HEALTH INFORMATION FOR INTERNATIONAL TRAVEL 2001-2002

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control and Prevention
National Center for Infectious Diseases
Division of Quarantine
Atlanta, Georgia

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PREFACE

One of the important responsibilities of the Centers for Disease Control and Prevention (CDC) is to provide up-to-date and comprehensive information on immunization requirements and recommendations for international travelers. This publication is one of the methods employed to help fulfill that responsibility.

The Travelers' Health Section of the Division of Quarantine, National Center for Infectious Diseases, gratefully acknowledges the contributions of all internal and external writers and reviewers and humbly acknowledges that, without their valuable assistance, this publication would not have been possible.

Readers are invited to send comments and suggestions regarding this publication to:

CENTERS FOR DISEASE CONTROL AND PREVENTION
National Center for Infectious Diseases
Division of Quarantine (E-03)
Attention: Travelers' Health Section
Atlanta, Georgia 30333

CENTERS FOR DISEASE CONTROL AND PREVENTION
Jeffrey P. Koplan, MD, MPH, *Director*

National Center for Infectious Diseases
James M. Hughes, MD, *Director*

Division of Quarantine
Tony D. Perez, BA, *Director*

Martin S. Cetron, MD
Deputy Director

Phyllis E. Kozarsky, MD, *Chief*
Travelers' Health

Rosamond R. Dewart, BA
Special Projects Manager

Julie A. Bettinger, MPH
Epidemiologist

Stefanie F. Steele, RN, MPH
Health Educator

Connie L. Whitehead, BA
Editor

CONTRIBUTORS

Addiss, David G., MD, MPH

Ashford, David A., DVM, DSc, MPH

Atkinson, William, MD

Beach, Michael J., PhD

Bern, Caryn, MD, MPH

Bisgard, Kristine, DVM, MPH

Bridges, Carolyn Buxton, MD

Burr, Roger, MD, MPH

Castro, Kenneth G., MD

Clark, Gary G., PhD

Craven, Robert B., MD

Dasch, Gregory A., PhD, MPH

DeMarcus, Thomas, MS

Duprey, Zandra L., DVM

Forney, David, BS

Freedman, David O., MD

Gage, Kenneth L., MD

Gilchrist, Julie, MD

Gubler, Duane J., ScD

Hayes, Edward B., MD

Herwaldt, Barbara, MD, MPH

Holmberg, Scott D., MD, MPH

James, Bruce H., MD, MPH

Juranek, Dennis D., DVM, MSc

Kamimoto, Laurie A., MD, MPH

Kaplan, Jonathan E., MD

Lackritz, Eve, MD

Maloney, Susan, MD, MHS

McGeehin, Michael A., PhD, MSPH

Mintz, Eric D., MD, MPH

Moore, Anne, MD, PhD

Moyer, Linda, RN, BS

Nichol, Stuart T., PhD

Olson, Sarah, CHES

Papania, Mark, MD, MPH

Parise, Monica, MD

Rogers, David, BS (BSIM)

Rollin, Pierre E., MD

Rosenstein, Nancy, MD

Rupprecht, Charles, VMD, MS, PhD

Ryan, Caroline A., MD, MPH

Schonberger, Lawrence, MD

Schulte, Joann, DO

Seward, Jane, MBBS, MPH

Shlim, David R., MD

Zanardi, Lynn, MD, MPH

Zimmerman, Laura, MPH

CONTENTS

Page

DISCLAIMER ii

PREFACE iii

CONTRIBUTORS v

LIST OF TABLES xi

LIST OF MAPS xiii

INTRODUCTION xv

CHANGES SINCE 1999–2000 EDITION xxi

CHAPTER 1—VACCINATION INFORMATION 1
- How To Use This Resource To Determine Vaccinations Required or Recommended 3
- Vaccination Certificate Requirements 3
- Model of a Correctly Completed Certificate 4
- Vaccination Certificate Requirements for Direct Travel From the United States To Other Countries 4
- U.S. Public Health Service Recommendations 6
- Vaccine Recommendations for Infants and Children 12

CHAPTER 2—YELLOW FEVER VACCINE REQUIREMENTS AND INFORMATION ON MALARIA RISK AND PROPHYLAXIS, BY COUNTRY 23

CHAPTER 3—SPECIFIC RECOMMENDATIONS FOR VACCINATIONS AND DISEASE PREVENTION 55
- Acquired Immunodeficiency Syndrome (AIDS) 57
- African Sleeping Sickness (African Trypanosomiasis) 59
- Amebiasis 60
- Bovine Spongiform Encephalopathy and New Variant Creutzfeldt-Jakob Disease 61
- Chagas' Disease (American Trypanosomiasis) 63
- Cholera 64
- Cryptosporidiosis 65
- Cyclosporiasis 66
- Dengue Fever 67

Diphtheria, Tetanus, and Pertussis 70
Encephalitis, Japanese 74
Encephalitis, Tickborne 81
Filariasis, Lymphatic 82
Giardiasis 83
Haemophilus Influenzae Type b Meningitis
and Invasive Disease 84
Hepatitis, Viral, Type A 86
Hepatitis, Viral, Type B 91
Hepatitis, Viral, Type C 96
Hepatitis, Viral, Type E 97
Influenza 98
Lassa Fever 102
Leishmaniasis 103
Leptospirosis 104
Lyme Disease 105
Malaria 106
Measles 121
Meningococcal Disease 124
Mumps 127
Onchocerciasis (River Blindness) 129
Plague 130
Poliomyelitis 131
Rabies 133
Rift Valley Fever 139
Rubella 139
Schistosomiasis 141
Sexually Transmitted Diseases (STDs) 142
Smallpox 144
Tetanus 144
Tuberculosis 144
Typhoid Fever 146
Typhus Fevers 149
Varicella (Chickenpox) 150
Yellow Fever 154

CHAPTER 4—HEALTH HINTS FOR THE INTERNATIONAL TRAVELER 161
Introduction 163
Motion Sickness 163
Protection Against Mosquitoes and Other Arthropod Vectors 163
Risks From Food and Drink 165
Travelers' Diarrhea 168
Cruise Ship Travel 175

Spraying Aircraft for Insects—Disinsection 177
Environmental Effects 177
Altitude Illness 178
Natural Disasters and Environmental Hazards 179
Chernobyl 180
Injuries 181
Animal-Associated Hazards 182
Swimming Precautions 183
Recreational Water 183
Emerging Infectious Diseases 184
Illness Abroad 184
Death Overseas 186
The Post-Travel Period 187
Animal Importation and Reentry 187

CHAPTER 5—GEOGRAPHIC DISTRIBUTION OF POTENTIAL HEALTH HAZARDS TO TRAVELERS 191
Africa 193
The Americas 195
Asia 198
Europe 201
Oceania 203

CHAPTER 6—ADVISING THE TRAVELER WITH SPECIAL NEEDS 205
General Information Regarding Human Immunodeficiency Virus and Travel 207
Pregnancy, Breast-Feeding, and Travel 211
Travelers With Disabilities 220
International Adoptions 221

ADDITIONAL RESOURCES 225

INDEX 227

LIST OF TABLES

Page

Table 1-1.—Suggested Intervals for Vaccines Containing Live Measles Virus After Administration of Immune Globulin 10

Table 1-2.—Recommended Accelerated Immunization Schedule for Traveling Infants and Children Who Start the Series Late or Who Are More Than 1 Month Behind in the Immunization Schedule 13

Table 1-3.—Recommended Childhood Immunization Schedule United States, January–December 2001 14

Table 1-4.—Recommended Immunization Schedule for People Older Than 7 Years of Age Not Vaccinated at the Recommended Time in Early Infancy 19

Table 1-5.—Minimum Age for Initial Vaccination and Minimum Interval Between Vaccine Doses, by Type of Vaccine 20

Table 3-1.—Risk of Japanese Encephalitis, by Country, Region, and Season 76

Table 3-2.—Japanese Encephalitis Vaccine 80

Table 3-3.—Recommended *Haemophilus influenzae* Type b (Hib) Routine Vaccination Schedule 85

Table 3-4.—Recommended Doses of HAVRIX® 89

Table 3-5.—Recommended Doses of VAQTA® 89

Table 3-6.—Immune Globulin for Protection Against Viral Hepatitis A 89

Table 3-7.—Recommended Doses of Currently Licensed Hepatitis B Vaccines 94

Table 3-8.—Drugs Used in the Prophylaxis of Malaria 114

Table 3-9.—Pediatric Prophylactic Doses of Malarone™ 116

Table 3-10.—Presumptive Treatment of Malaria 118

Table 3-11.—Meningococcal Vaccine 127

Table 3-12.—Countries and Political Units Reporting No Cases of Rabies During 1997 and 1998 135

Table 3-13.—Criteria for Preexposure Immunization 136

Table 3-14.—Preexposure Immunization 137

Table 3-15.—Postexposure Immunization 138

Table 3-16.—Dosage and Schedule for Typhoid Fever Vaccination 148

Table 3-17.—Common Adverse Reactions to Typhoid Fever 148

Table 3-18.—Yellow Fever Vaccine 155

Table 4-1.—Treatment of Water With Tincture of Iodine 167

Table 4-2.—Composition of World Health Organization Oral Rehydration Solution (ORS) for Diarrheal Illness 174

Table 4-3.—Assessment of Dehydration Levels in Infants 175

Table 6-1.—Relative Contraindications to International Travel During Pregnancy 213

Table 6-2.—Vaccination During Pregnancy 215

Table 6-3.—Half-Lives of Selected Antimalarial Drugs 219

LIST OF MAPS

Page

Map 3-1.—World Distribution of Dengue, 2000 68

Map 3-2.—Anti-HAV Prevalence, 2000 87

Map 3-3.—Geographic Distribution of Hepatitis B Prevalence, 2000 92

Map 3-4.—Malaria Endemic Countries, 2000 108

Map 3-5.—Areas With Frequent Epidemics of Meningococcal Meningitis, 2000 126

Map 3-6.—Yellow Fever Endemic Zones in Africa, 2000 156

Map 3-7.—Yellow Fever Endemic Zones in the Americas, 2000 157

INTRODUCTION

This book is published by the Division of Quarantine (DQ), National Center for Infectious Diseases, Centers for Disease Control and Prevention (CDC), as a reference for those who advise international travelers of health risks. It is written primarily for health care providers, although others who advise travelers, such as travel agencies, airlines, cruise lines, missionary organizations, and academic institutions, might find the information useful. Additional information, as well as an online version of this text, can be found on the CDC Internet website at http://www.cdc.gov/travel. Regional and disease-specific documents may be requested from the CDC Fax Information Service at 1-888-CDC-FAXX (232-3299); the directory of international travel documents is available by request from the same number. Users who are not medical professionals might find these sources to be more user friendly. All these resources specify the vaccinations required by different countries and include information on preventive measures that travelers should take to protect their health.

A biennial publication such as this cannot remain absolutely current, given the speed of global travel and disease transmission. Therefore, this text should be used in conjunction with the electronic sources mentioned previously. Notices about changes in vaccine requirements, disease outbreaks, drug availability, or emerging infections will be posted promptly on these services. Any changes should be written into or filed in the corresponding sections of this book to keep the information up to date.

While this edition has been extensively reorganized to facilitate its use, it cannot cover *all* of the topics pertinent to the growing field of travel medicine. Instead, it continues to focus on the prevention of infectious diseases. Nonetheless, with the recognition that other conditions and illnesses might have a great impact on the health of travelers, several topics have been added or supplemented. New sections have been included on altitude sickness, international adoptions, and cruise ship travel. Moreover, for the first time, experts outside CDC have contributed to the writing and editing of entries in this text, especially for those particular health risks which no division within the agency is currently studying. There will always be issues not covered by this text that remain important to the maintenance of healthy travel. Therefore, this book must be viewed as just one reference of the many needed by those who counsel travelers.

Other sources of travel medicine information are the web sites of two professional medical organizations: the International Society of Travel Medicine at http://www.istm.org/ and the American Society of Tropical Medicine and Hygiene at http://www.astmh.org/. Both of these websites include directories of travel clinics throughout the United States. For travelers visiting other countries in the Western Hemisphere, the Pan American Health Organization (PAHO), a regional office of the World Health Organization (WHO), has a website at http://www.paho.org that includes country-specific information about many health issues. The WHO web address at http://www.who.int/ provides general information, as well as disease surveillance data worldwide. Another valuable resource for country information is the U.S. Central Intelligence Agency's website at http://www.odci.gov/cia/publications/pubs.html (select "World Factbook").

CDC's recommendations for international travelers apply primarily to vaccinations and prophylactic measures for U.S. travelers planning to visit areas of the world where diseases such as measles, poliomyelitis, typhoid fever, yellow fever, viral hepatitis, and malaria occur. The purpose of the International Health Regulations (IHRs) adopted by WHO is to ensure maximum security against the international spread of disease, with minimum interference with world commerce. As a result of these regulations, some countries require an International Certificate of Vaccination against yellow fever as a condition for entry. Because some countries require vaccination against yellow fever only if travelers arrive from a country infected with the disease, current information must be taken into consideration in determining whether vaccinations are required. DQ publishes a biweekly "Summary of Health Information for International Travel" (the "Blue Sheet") to show where cholera and yellow fever are being reported. The Blue Sheet is available by fax by calling 1-888-CDC-FAXX (232-3299) and requesting document number 220022; it can also be accessed online at http://www.cdc.gov/travel/blusheet.htm. Official changes in the vaccines required by individual countries and reported by WHO are reported in the Blue Sheet. These changes should be entered in the "Vaccination Certificate Requirements" section (page 3) of this book to keep information current. This book, when kept up to date with changes in vaccination requirements and used in conjunction with the Blue Sheet, provides accurate information on vaccinations required for international travel.

The extent to which advisory statements can be made specific for each country and each disease is limited by both space and the lack of reliable data. Although WHO regularly publishes data on the occurrence of many of these diseases, these figures represent only a small percentage of the actual number of cases. Communicable diseases are not reported consistently by practicing physicians, and many cases might never come to medical attention. For these reasons, any recommendations must be interpreted with care.

In general, the risk of acquiring illness when engaging in international travel depends on the areas of the world to be visited. Travelers to developing countries are at greater risk than those who travel to developed areas. In most developed countries (for example, Canada, Australia, New Zealand, Japan, and western Europe), the risk to the general health of the traveler is no greater than that incurred throughout the United States. Living conditions and standards of sanitation and hygiene vary considerably throughout the world, and in developing nations immunization coverage levels can be low; thus, the risk of acquiring disease can vary greatly in these locations. Travelers visiting primarily tourist areas, on itineraries that do not include visits to rural areas, have a lower risk of exposure to contaminated food or water.

Travelers who visit small cities off the usual tourist routes, who spend extended periods of time in small villages or rural areas, or who expect to have prolonged contact with children are at greater risk of acquiring infectious diseases because of exposure to water and food of poor quality and close contact with local residents who might not appear ill but still might harbor organisms that cause such diseases. Consequently, the added protection of booster or additional doses of certain vaccines and other prophylaxis is recommended for these people. International travelers should be advised to contact their physicians, local health departments, or private or public agencies that advise

international travelers at least 6 weeks prior to departure to obtain current health information on the countries they plan to visit. See Chapter 3, "Specific Recommendations for Vaccinations and Disease Prevention" for more detailed comments.

In addition to geographic-specific risk factors, host susceptibility factors can play a significant role in determining the risk of acquiring illness during international travel. People at the extremes of age (young children and the elderly), pregnant women, or immunocompromised (for example, human immunodeficiency virus-infected) people can be particularly vulnerable to certain infectious diseases. It is strongly advised that these people contact physicians with special expertise in travel medicine at least 6 weeks before departure, especially if the itinerary includes high-risk destinations.

LIST OF COUNTRIES BY REGION

To facilitate the use of this book, the following list of countries and other areas by region is provided. These regions correspond with those used by CDC's Fax Information Service for international travel. For region-specific vaccine recommendations and requirements, a directory of international documents may be requested at 1-888-CDC-FAXX (232-3299).

AFRICA

North Africa

Algeria
Canary Islands
Egypt
Libya
Morocco
Tunisia

Southern Africa

Botswana
Lesotho
Namibia
Saint Helena
South Africa
Swaziland

Central Africa

Angola
Cameroon
Central African Republic
Chad
Congo
Democratic Republic of the Congo
Equatorial Guinea
Gabon
Sudan
Zambia
Zimbabwe

East Africa

Burundi
Comoros
Djibouti
Eritrea
Ethiopia
Kenya
Madagascar
Malawi
Mauritius
Mayotte
Mozambique
Réunion
Rwanda
Seychelles
Somalia
Tanzania
Uganda

West Africa

Benin
Burkina Faso
Cape Verde Islands
Côte d'Ivoire
The Gambia
Ghana
Guinea
Guinea-Bissau
Liberia
Mali
Mauritania
Niger
Nigeria
São Tomé and Principe
Senegal
Sierra Leone
Togo

THE AMERICAS

Mexico and Central America

Belize
Costa Rica
El Salvador
Guatemala
Honduras
Mexico
Nicaragua
Panama

North America

Canada
Greenland
Saint Pierre and Miquelon
United States

Tropical South America

Bolivia
Brazil
Colombia
Ecuador
French Guiana
Guyana
Paraguay
Peru
Suriname
Venezuela

Temperate South America

Argentina
Chile
Falkland Islands (U.K.)
Uruguay

THE CARIBBEAN

Anguilla (U.K.)
Antigua and Barbuda
Aruba
Bahamas
Barbados
Bermuda (U.K.)
Cayman Islands (U.K.)
Cuba
Dominica
Dominican Republic
Grenada
Guadeloupe
Haiti
Jamaica
Martinique (Fr.)
Montserrat (U.K.)
Netherlands Antilles: Bonaire, Curaçao, Saba, Saint Eustatius, Sint Maarten
Puerto Rico (U.S.)
Saint Lucia
Saint Kitts (Saint Christopher) and Nevis (U.K.)
Saint Vincent and the Grenadines
Turks and Caicos (U.K.)
Trinidad and Tobago
Virgin Islands, U.S., U.K

ASIA

East Asia

China (including Hong Kong and Macao)
Japan
Mongolia
North Korea
South Korea

Southeast Asia

Brunei
Burma (Myanmar)
Cambodia
Indonesia
Laos
Malaysia
Philippines
Singapore
Thailand
Vietnam

Indian Subcontinent

Afghanistan
Bangladesh
Bhutan
India
Maldives
Nepal
Pakistan
Sri Lanka

Middle East

Bahrain
Cyprus
Iran
Iraq
Israel
Jordan
Kuwait
Lebanon
Oman
Qatar
Saudi Arabia
Syria
Turkey
United Arab Emirates
Yemen

West Central Asia

Kazakhstan
Kyrgyzstan
Tajikistan
Turkmenistan
Uzbekistan

EUROPE

Eastern Europe

Albania
Armenia
Azerbaijan
Belarus
Bosnia and Herzegovina
Bulgaria
Croatia
Czech Republic
Estonia
Former Yugoslav Republic of Macedonia
Georgia
Hungary
Latvia
Lithuania
Moldova
Poland
Romania
Russia
Slovakia
Slovenia
Ukraine
Yugoslavia

Western Europe

Andorra
Austria
Azores
Belgium
Denmark
Faroe Islands
Finland
France
Germany
Gibraltar
Greece
Greenland
Iceland
Ireland
Italy
Liechtenstein
Luxembourg
Madeira
Malta
Monaco
Netherlands
Norway
Portugal
San Marino
Spain
Sweden
Switzerland
United Kingdom

OCEANIA

Australia

Antarctica

Melanesia and Micronesia–Polynesia

American Samoa
Christmas Island
Cook Island
Easter Island
Fiji
French Polynesia
Guam
Kiribati
Micronesia (Federated States of)
Marshall Islands
Nauru
New Caledonia
Niue
Northern Mariana Islands
Palau
Papua New Guinea
Pitcairn Island
Samoa
Solomon Islands
Tahiti
Tonga
Tokelau
Tuvalu
U.S. Trust Territories
Vanuatu
Wake Island (U.S.)
Wallis and Futuna

CHANGES FOR THE 2001–2002 EDITION OF THE YELLOW BOOK

GENERAL

! New, improved maps and indexing have been included, as well as an updated country listing for malaria and yellow fever information.

! Although this publication is available to the general public, its primary audience is health care providers and those working in the field of travel medicine.

! Age categories for infants, children, adolescents, and adults have been standardized *for this publication*. They are:

Infant —24 months of age or younger	Child — 2 through 12 years
Adolescent — 13 through 17 years	Adult — 18 years of age or older

CHAPTER SPECIFIC

! **Chapter 1—Vaccination Information**

- The entire text for this chapter has been updated and revised to reflect current standards and information.

! **Chapter 2—Yellow Fever Vaccine Requirements and Information on Malaria Risk and Prophylaxis, by Country**

- An updated list of countries that require an international certificate of vaccination is included. Readers should refer to the Blue Sheet (*Summary of Health Information for International Travel*) (available online at http://www.cdc.gov/travel/blusheet.htm) for the most current information.

- Updated information on malaria risk by country and areas with chloroquine-resistant *Plasmodium falciparum* is provided. (Specific prophylaxis regimes can be found in Chapter 3, "Specific Recommendations for Vaccinations and Disease Prevention," "Malaria," pages 106 through 120.)

! **Chapter 3—Specific Recommendations for Vaccinations and Disease Prevention**

- All disease-specific text and accompanying tables and maps have been updated and revised.

- Additional or new (as applicable) information is provided on bovine spongiform encephalopathy, hepatitis, and poliomyelitis.

- The “Malaria” section includes recommendations for the use of Malarone®.

! **Chapter 4—Health Hints for the International Traveler**

- Additional information is included in the section on “Altitude Sickness” (pages 178 and 179).

- Additional guidance on cruise ship travel immunizations is provided.

! **Chapter 5—Geographic Distribution of Potential Health Hazards**

- The text for disease risks has been completely updated.

- Geographic divisions reflect those used by the Centers for Disease Control and Prevention.

! **Chapter 6—Advising the Traveler With Special Needs**

- All text and accompanying tables have been updated and revised.

- A new section on “International Adoptions” (pages 221 through 224) is included.

CHAPTER 1

VACCINATION INFORMATION

How To Use This Resource To Determine Vaccinations Required or Recommended

The following steps are suggested to determine vaccination requirements.

1. The traveler should be advised to list his or her itinerary in the sequence in which countries will be visited. The length of stay in each country also should be considered. For the purpose of the International Health Regulations, the incubation periods of the quarantinable diseases are:

   - Cholera — 5 days
   - Plague — 6 days
   - Yellow fever — 6 days

2. Health care providers should use Chapter 2, "Yellow Fever Vaccine Requirements and Information on Malaria Risk and Prophylaxis, by Country" (yellow pages) to determine the yellow fever vaccination requirements for each country. Because some countries require vaccination only if a traveler arrives from an infected area, health care providers should check the current biweekly *Summary of Health Information for International Travel* (also known as the Blue Sheet) to determine if any country on the itinerary is currently infected with yellow fever. The Blue Sheet is available both from the Centers for Disease Control and Prevention (CDC) website at http://www.cdc.gov/travel/blusheet.htm and from the CDC Fax Information Service by telephoning 1-888-CDC-FAXX (232-3299) and requesting document number 220022.

Most immunizations are not required under the International Health Regulations, but are recommended to protect the health of the traveler. Health care providers should consider inoculating the traveler for the following diseases: tetanus, diphtheria, pertussis, poliomyelitis, measles, hepatitis A, hepatitis B, varicella, Japanese encephalitis, meningococcal meningitis, rabies, typhoid fever, and yellow fever. For those diseases for which no vaccines are available, specific preventive behaviors or medications are a necessity. Chapter 3, "Specific Recommendations for Vaccinations and Disease Prevention," pages 55 through 160, provides detailed immunization and prophylaxis information for a variety of diseases. Subsequent chapters address the special needs of potentially at-risk or high-risk travelers, including infants, children, pregnant women, and those with compromised immune systems. Because the recommendations in this publication can change because of outbreaks or other events (such as natural disasters), travelers should be advised either to contact the CDC Fax Information Service (request document number 000005) or to consult the CDC Travelers' Health website at http://www.cdc.gov/travel for the most up-to-date information.

Vaccination Certificate Requirements

Under the International Health Regulations adopted by the World Health Organization, a country may, under certain conditions, require an International Certificate of Vaccination against yellow fever from international travelers.

The World Health Assembly amended the International Health Regulations in 1973 so that cholera vaccination is no longer required of any traveler. As a result, no country requires a certificate of cholera immunization and, indeed, cholera vaccine is no longer available in the United States.

MODEL OF A CORRECTLY COMPLETED CERTIFICATE

An International Certificate of Vaccination must be complete in every detail; if incomplete or inaccurate, it is not valid. Revisions of this certificate dated 9-66, 9-69, 9-71, 1-74, 9-77, 1-82, or 11-91 are acceptable.

INTERNATIONAL CERTIFICATE OF VACCINATION
AS APPROVED BY
THE WORLD HEALTH ORGANIZATION

CERTIFICAT INTERNATIONAL DE VACCINATION
APPROUVÉ PAR
L'ORGANISATION MONDIALE DE LA SANTÉ

Jane Doe
TRAVELER'S NAME–NOM DU VOYAGEUR

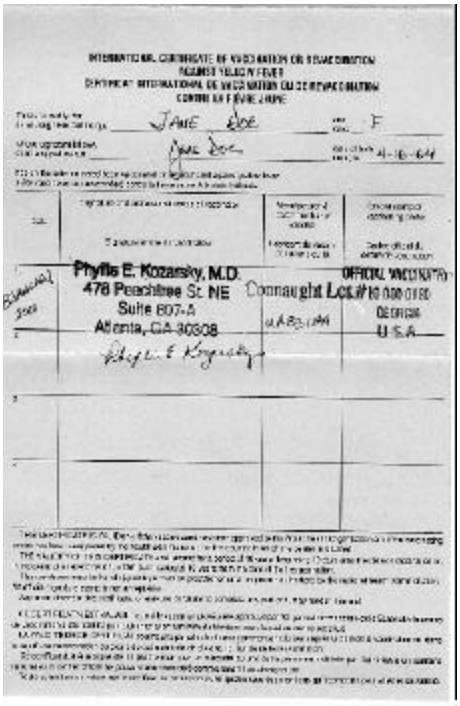
123 Clairmont Road
ADDRESS–ADRESSE (Number–Numéro) (Street–Rue)

Atlanta, Georgia 30029
(City–Ville)

Fulton USA
(County–Département) (State–Etat)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

PHS–731 (REV.11-91)


Phyllis E. Kozarsky, M.D.
478 Peachtree St. NE
Suite 807-A
Atlanta, GA 30308
Connaught Lot
OFFICIAL VACCINATOR
GEORGIA
U.S.A.

A copy of the International Certificate of Vaccination, PHS-731, may be purchased for $1.00 ($15.00 per 100) from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, telephone 1-202-512-1800. The stock number is 017-001-00483-9.

VACCINATION CERTIFICATE REQUIREMENTS FOR DIRECT TRAVEL FROM THE UNITED STATES TO OTHER COUNTRIES

For direct travel from the United States, only the following countries require an International Certificate of Vaccination against yellow fever.

Benin
Burkina Faso
Cameroon
Central African Republic
Congo
Côte d'Ivoire
Democratic Republic of the Congo
French Guiana
Gabon
Ghana
Liberia
Mali
Mauritania (for a stay of more than 2 weeks)
Niger
Rwanda
São Tomé and Principe
Togo

For travel to and between other countries, individual country requirements should be checked. **Currently, no vaccinations are required to return to the United States.**

Exemption From Vaccination

Age: Some countries do not require an International Certificate of Vaccination for infants younger than 6 months of age or 1 year of age. Travelers should be advised to check the individual country requirements in Chapter 2, "Yellow Fever Vaccine Requirements and Information on Malaria Risk and Chloroquine resistance, by Country," pages 23 through 54.

Medical Grounds: If a physician concludes that a particular vaccination should not be administered for medical reasons, the traveler should be given a signed and dated statement of the reasons on the physician's letterhead stationary.

There are no other acceptable reasons for exemption from vaccination.

Unvaccinated Travelers

Travelers who do not have the required vaccinations upon entering a country might be subject to vaccination, medical followup, or isolation, or a combination of these. In a few countries, unvaccinated travelers are denied entry.

Travel on Military Orders

Because military requirements may exceed the requirements indicated in this publication, any person who plans to travel on military orders (civilians and military personnel) should be advised to contact the nearest military medical facility to determine the requirements for the trip.

Authorization To Provide Vaccinations and To Validate the International Certificate of Vaccination

A yellow fever vaccination must be given at an official yellow fever vaccination center as designated by respective state health departments or the Division of Quarantine, Centers for Disease Control and

Prevention, and the accompanying certificate must be validated by the center that administers the vaccine. (Other vaccinations may be given under the supervision of any licensed physician.) Validation of the certificate can be obtained at most city, county, and state health departments, or from vaccinating physicians who possess a "Uniform Stamp." State health departments are responsible for designated nonfederal yellow fever vaccination centers and issuing Uniform Stamps to be used to validate the International Certificate of Vaccination. Information about the location and hours of yellow fever vaccination centers may be obtained by contacting local or state health departments. Physicians administering vaccine to travelers should emphasize that an International Certificate of Vaccination must be validated to be acceptable to quarantine authorities. Failure to secure validations can cause a traveler to be revaccinated, quarantined, or denied entry.

People Authorized To Sign the Certificate

The International Certificate of Vaccination must be signed by a licensed physician or by a person designated by the physician. A signature stamp is not acceptable.

U.S. PUBLIC HEALTH SERVICE RECOMMENDATIONS

General Recommendations on Vaccination and Prophylaxis

The Advisory Committee on Immunization Practices (ACIP) makes immunization recommendations to the U.S. Public Health Service. Benefits and risks are associated with the use of all immunobiologics—no vaccine is completely effective or completely free of side effects. The recommendations are based on scientific evidence of benefits and risks to achieve optimal levels of protection against vaccine-preventable diseases. The recommendations include information on general immunization issues and on the use of specific vaccines. When these recommendations are issued or revised, they are published in the *Morbidity and Mortality Weekly Report* (http://www.cdc.gov/mmwr).

Vaccinations against diphtheria, tetanus, pertussis, measles, mumps, rubella, varicella, poliomyelitis, hepatitis B, *Haemophilus influenzae* type b, and pneumococcal invasive disease are routinely administered in the United States, usually in childhood. If people do not have a history of adequate protection against these diseases, immunizations appropriate to their age and previous immunization status should be obtained, whether or not international travel is planned. The childhood vaccination schedule changes annually and recommendations for adolescents and adults change often. Immunization providers should obtain the most current schedules from the National Immunization Program website at http://www.cdc.gov/nip. The text and Tables 1-1 through 1-5, 3-1 through 3-7, 3-11, 3-13 through 3-18, and 6-2 of this publication present recommendations for the use, number of doses, dose intervals, boosters, adverse reactions, precautions, and contraindications of vaccines and toxoids that may be indicated for travelers. For specific vaccines and toxoids, additional details on background, adverse reactions, precautions, and contraindications are found in the appropriate ACIP statements.

Spacing of Immunobiologics

Multiple Doses of the Same Antigen

Some vaccines require more than one dose for adequate protection. The use of multiple reduced doses or the use of doses given at less than minimum intervals can lessen the antibody response and is not endorsed or recommended; such doses should not be counted as part of the vaccination series. The minimum interval between subsequent doses of vaccine is shown in Table 1-5. **Except for oral typhoid vaccine, it is unnecessary to restart an interrupted series of a vaccine or toxoid or to add extra doses.** However, some products (tetanus and diphtheria toxoids) require periodic booster doses to maintain protection.

Simultaneous Administration

All commonly used vaccines can safely and effectively be given simultaneously (that is, on the same day) without impairing antibody responses or increasing rates of adverse reactions. This is particularly helpful for international travelers for whom exposure to several infectious diseases might be imminent.

In general, inactivated vaccines may be administered simultaneously at separate sites. However, when vaccines commonly associated with local or systemic reactions are given simultaneously, reactions can be accentuated. It is preferable to administer these vaccines on separate occasions.

Simultaneous administration of acellular pertussis (DTaP); inactivated poliovirus (IPV); *Haemophilus influenzae* type b (Hib); measles, mumps, and rubella (MMR); varicella; pneumococcal conjugate; and hepatitis B vaccines is encouraged for those who are the recommended age to receive these vaccines and for whom no contraindications exist at the time.

Yellow fever vaccine may be administered simultaneously with all other currently available vaccines.

Limited data suggest that the immunogenicity and safety of Japanese encephalitis (JE) vaccine are not compromised by simultaneous administration with DTaP or whole-cell pertussis (DTP) vaccine. No data exist on the effect of concurrent administration of other vaccines, drugs (for example, chloroquine or mefloquine), or biologicals on the safety and immunogenicity of JE vaccine.

Inactivated vaccines generally do not interfere with the immune response to other inactivated or live virus vaccines. An inactivated vaccine may be given either simultaneously or at any time before or after a different inactivated vaccine or a live virus vaccine.

The immune response to an injected live virus vaccine (for example, MMR, varicella, or yellow fever) might be impaired if administered within 28 days of another live virus vaccine. Whenever possible, injected live virus vaccines administered on different days should be administered at least 28 days

apart. If two injected live virus vaccines are not administered on the same day but less than 28 days apart, the second vaccine should be readministered 4 weeks or more later.

Live virus vaccines can interfere with an individual's response to tuberculin testing. Tuberculin testing, if otherwise indicated, can be done on the day that live virus vaccines are administered or 4 to 6 weeks later.

Vaccination of People With Acute Illnesses

It is important to take every opportunity to provide appropriate vaccinations. The decision to delay vaccination because of a current or recent acute illness depends on the severity of the symptoms and their etiology. Although a moderate or severe acute illness is sufficient reason to postpone vaccination, minor illnesses (such as diarrhea, mild upper respiratory infection with or without low-grade fever, or other low-grade febrile illness) are not contraindications to vaccination. Antimicrobial therapy is not a contraindication to vaccination, except in some circumstances with oral typhoid vaccine (Ty21a). People with moderate or severe acute illness with or without fever should be vaccinated as soon as their condition has improved. This precaution is to avoid superimposing adverse effects from the vaccine on underlying illness or mistakenly attributing a manifestation of underlying illness to the vaccine.

Routine physical examinations or temperature measurements are not prerequisites for vaccinating anyone who appears to be in good health. Asking if a person is ill, postponing a vaccination for someone with moderate or severe acute illness, and vaccinating someone without contraindications are appropriate procedures in immunization programs.

Immune Globulin (IG) Preparations

When MMR and varicella vaccines are given with immune globulin (IG, formerly called immune serum globulin and immunoglobulin) preparations, antibody response can be diminished. IG preparations do not interfere with the immune response to yellow fever vaccine. The duration of inhibition of MMR and varicella vaccines is related to the dose of IG. Administration of MMR or its components and of varicella vaccines should be delayed for 3 to 11 months after IG administration, depending on the type and quantity administered. Recommended intervals are shown in Table 1-1.

Immune globulin administration may become necessary after MMR or its individual components and varicella vaccines have been given, and interference can occur. Vaccine virus replication and stimulation of immunity usually occur within 2 to 3 weeks after vaccination. If the interval between administration of one of these vaccines and the subsequent administration of an IG preparation is at least 14 days, the vaccine need not be readministered. If the interval is less than 14 days, the vaccine should be readministered after the interval shown in Table 1-1, unless serologic testing indicates that antibodies have been produced. If administration of immune globulin becomes necessary, MMR or its components and varicella vaccines can be administered simultaneously with IG, with the recognition that vaccine-induced immunity can be compromised. The vaccine should be administered

in a site remote from that chosen for the IG injection. Vaccination should be repeated after the interval noted in Table 1-1, unless serologic testing indicates antibodies have been produced.

When IG is given with the first dose of hepatitis A vaccine (HAV), the proportion of people who develop protective levels of antibody is not affected, but antibody concentrations are lower. Because the final concentrations of anti-HAV are many times higher than those considered protective, this reduced immunogenicity is not expected to be clinically important. IG preparations interact minimally with other inactivated vaccines and toxoids. Therefore, other inactivated vaccines may be given simultaneously or at any time interval after or before an antibody-containing blood product is used. However, such vaccines should be administered at different sites.

Hypersensitivity to Vaccine Components

Vaccine components can cause allergic reactions in some recipients. These reactions can be local or systemic and can include anaphylaxis or anaphylactic-like responses. The vaccine components responsible can include the vaccine antigen, animal proteins, antibiotics, preservatives, or stabilizers. The most common animal protein allergen is egg protein in vaccines prepared using embryonated chicken eggs (influenza and yellow fever vaccines). Generally, people who are able to eat eggs or egg products safely may receive these vaccines, while people with histories of anaphylactic allergy (for example, hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) to eggs or egg proteins ordinarily should not. Screening people by asking whether they can eat eggs without adverse effects is a reasonable way to identify those who might be at risk from receiving yellow fever and influenza vaccines. Recent studies have indicated that there are other components in vaccines in addition to egg proteins (for example, gelatin) that might cause allergic reactions, including anaphylaxis in rare instances. Protocols have been developed for testing and vaccinating people with anaphylactic reactions to egg ingestion.

Some vaccines contain preservatives (for example, thimerosal, a mercury compound) or trace amounts of antibiotics to which people might be allergic. Those administering the vaccine(s) should carefully review the information provided in the package insert before deciding if the rare person with such allergy should receive the vaccine(s). No currently recommended vaccine contains penicillin or penicillin derivatives. Some vaccines (for example, MMR and its individual component vaccines) contain trace amounts of neomycin or other antibiotics; the amount is less than would normally be used for the skin test to determine hypersensitivity. However, people who have experienced anaphylactic reactions to the antibiotic generally should not receive these vaccines. Most often, neomycin allergy is a contact dermatitis—a manifestation of a delayed-type (cell-mediated) immune response—rather than anaphylaxis. A history of delayed-type reactions to neomycin is not a contraindication to receiving these vaccines.

Reporting Adverse Events Following Immunization

Modern vaccines are extremely safe and effective. However, adverse events following immunization have been reported with all vaccines. These range from frequent, minor, local reactions to extremely

Table 1-1.—Suggested Intervals for Vaccines Containing Live Measles Virus After Administration of Immune Globulin.*

INDICATION	DOSE	SUGGESTED INTERVAL BEFORE MEASLES VACCINATION
Tetanus (TIG)	250 units (10 mg IgG/kg) IM	3 months
Hepatitis A (IG) International Travel		
3 months or less	0.02 mL/kg(3.3 mg IgG/kg) IM	3 months
More than 3 months	0.06 mL/kg (10 mg IgG/kg) IM	3 months
Hepatitis B prophylaxis (HBIG)	0.06 mL/kg (10 mg IgG/kg) IM	3 months
Rabies prophylaxis (HRIG)	20 IU/kg (22 mg IgG/kg) IM	4 months
Varicella prophylaxis (VZIG)	125 units/10kg (20 to 40 mg IgG/kg) IM (maximum 625 units)	5 months
Measles prophylaxis (IG)		
Normal contact	0.25 mL/kg (40 mg IgG/kg) IM	5 months
Immunocompromised contact †	0.50 mL/kg (80 mg IgG/kg) IM	6 months
Blood Transfusion		
Red blood cells (RBCs), washed	10 mL/kg (negligible IgG/kg) IV	None
RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3 months
Packed RBCs (Hct 65%)§	10 mL/kg (60 mg IgG/kg) IV	6 months
Whole blood (Hct 35% to 50%)§	10 mL/kg (80 to 100 mg IgG/kg) IV	6 months
Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7 months
Cytomegalovirus prophylaxis (CMV IGIV)	150 mg/kg (maximum)	6 months
Respiratory syncytial virus (RSV) monoclonal antibody (Synagis™)¶	15 mg/kg IM	None

RSV prophylaxis (RSV IGIV)	750 mg/kg	9 months
Intravenous Immune Globulin (IGIV)		
IGIV, Replacement therapy	300 to 400 mg/kg IV	8 months
IGIV, ITP**	400 mg/kg IV	8 months
IGIV, ITP**	1,000 mg/kg IV	10 months
IGIV, Kawasaki disease	2 grams/kg IV	11 months

Abbreviated forms used in table: mg - milligram; kg - kilogram; Ig - immune globulin; IM -intramuscular; mL - milliliter; IU - international unit; IV - intravenous.

*This table is not intended to be used to determine the correct indications and dosage for the use of IG preparations. Unvaccinated people might not be fully protected against measles during the entire suggested interval, and additional doses of IG or measles, or both, vaccines may be indicated following measles exposure. The concentration of measles antibody in a particular IG preparation can vary by lot. The rate of antibody clearance following receipt of an IG preparation can also vary. The recommended intervals are extrapolated from an estimated half-life of 30 days for passively acquired antibody and an observed interference with the immune response to measles vaccine for 5 months following a dose of 80 mg IgG/kg.

†Measles vaccination is recommended for children with human immunodeficiency virus (HIV) infection but is contraindicated in patients with congenital disorders of the immune system.

§ Assumes a serum IgG concentration of 16 mg/mL.

¶Contains only antibody to respiratory syncytial virus.

**Immune (formerly, idiopathic) thrombocytopenic purpura.

rare, severe, systemic illness such as paralysis associated with oral poliovirus (OPV). Information on side effects and adverse events following specific vaccines and toxoids are discussed in detail in each ACIP statement. Health care providers are required by law to report selected adverse events occurring after vaccination with DTaP, diphtheria-tetanus (DT), tetanus-diphtheria (Td), MMR, measles-rubella (MR), measles, OPV, IPV, varicella, Hib, hepatitis B, and yellow fever vaccines. (Reportable events are listed in MMWR 1988;37(13):197-200 and, in general, are events usually requiring the recipient to seek medical attention.) These events and all temporally associated events following receipt of all other vaccines severe enough to require the recipient to seek medical attention should be reported to the Vaccine Adverse Event Reporting System (VAERS) (1-800-822-7967) maintained by the Centers for Disease Control and Prevention and the U.S. Food and Drug Administration.

VACCINE RECOMMENDATIONS FOR INFANTS AND CHILDREN

Age at Which Immunobiologics Are Administered

Factors that influence recommendations concerning the age at which a vaccine is administered include the age-specific risks of the disease and its complications, the ability of people of a given age to respond to the vaccine, and the potential interference with the immune response by passively transferred maternal antibody. Vaccines are recommended for the youngest age group at risk of developing the disease whose members are known to develop an adequate antibody response to vaccination.

The routine immunization recommendations and schedules for infants and children in the United States (Tables 1-2 and 1-3) do not provide specific guidelines for infants and young children who will travel internationally before the age when specific vaccines and toxoids are routinely recom-mended. The following section, “Immunization Schedule Modifications for International Travel for Inadequately Immunized Infants and Younger Children,” provides revised recommendations and schedules for active and passive immunization of such infants and children.

Immunization Schedule Modifications for International Travel for Inadequately Immunized Infants and Younger Children

Routine Infant and Childhood Vaccine-Preventable Diseases (Diphtheria, Tetanus, Pertussis, Measles, Mumps, Rubella, Varicella, Polio, *Haemophilus Influenzae* Type b, and Hepatitis B)

Diphtheria and Tetanus Toxoid and Pertussis Vaccine

Diphtheria is an endemic disease in many developing countries and has been found in the independent countries of the former Soviet Union. Tetanus occurs worldwide.

Table 1-2.—Recommended Accelerated Immunization Schedule for Traveling Infants and Children Who Start the Series Late* or Who Are More Than 1 Month Behind in the Immunization Schedule† (Children for Whom Compliance With Scheduled Return Visits Cannot Be Assured).

TIMING	VACCINES	COMMENTS
First visit (4 months of age or older)	DTaP, IPV, Hib§, hepatitis B, MMR, varicella, pneumococcal conjugate vaccine (PCV7)	Must be 12 months of age or older to receive MMR and varicella. If 5 years of age or older, Hib is not normally indicated. The PCV7 schedule varies by when the vaccination series is started.†
Second visit (1 month after first visit)	DTaP, IPV, Hib§, hepatitis B	None.
Third visit (1 month after second visit)	DTaP, IPV, Hib§	None.
Fourth visit (6 months or more after third visit)	DTaP, Hib§, hepatitis B	None.
4 to 6 years of age	DTaP, IPV, MMR	Preferably at or before school entry. DTaP is not necessary if fourth dose is given on or after the fourth birthday. IPV is not necessary if third dose is given on or after fourth birthday.
11 to 12 years of age	MMR, varicella, and/or hepatitis B, tetanus and diphtheria toxoids	Td should be given if more than 5 years since last dose. Repeat Td every 10 years throughout life. Hepatitis B should be given if not already received.

Abbreviated forms used in table: DTaP - acellular pertussis; IPV - inactivated poliovirus; Hib - *Haemophilus influenzae* type b; MMR - measles, mumps, and rubella; Td - tetanus-diphtheria.

Based on *General Recommendation on Immunization* (1994), with modifications from subsequent Advisory Committee on Immunization Practices (ACIP) statements.

*If initiated in the first year of life, administer DTaP doses one through three and polio doses one through three according to this schedule; administer MMR and varicella when the infant reaches 12 to 15 months of age. All vaccines should be administered simultaneously at the appropriate visit.

†See individual ACIP recommendations for detailed information on specific vaccines.

§Recommended Hib schedule varies by vaccine manufacturer and age of the child when vaccination series is started. If series is begun when the infant is younger than 6 months of age, four doses are needed. Only three doses are needed if all doses are PRP-OMP (PedVaxHIB®), Merck & Co., Inc.). The fourth dose must be at least 2 months after the third dose and on or after the infant's first birthday. If the series is started when the infant is 7 to 11 months of age, three doses are needed, with the third dose 2 months after the second dose and on or after the first birthday. If series is started when the infant is 12 to 14 months of age, two doses are needed, 2 months apart. If series is started when the infant is 15 months of age or older, one dose of any licensed conjugate Hib vaccine is recommended.

Table 1-3.—Recommended Childhood Immunization Schedule United States, January - December 2001.

Vaccines[1] are listed under routinely recommended ages. Bars indicate the range of recommended ages for immunization. Any dose not given at the recommended age should be given as a "catch-up" immunization at any subsequent visit when indicated and feasible. Ovals indicate vaccines to be given if previously recommended doses were missed or given earlier than the recommended minimum age.

Age ▶ / Vaccine ▼	Birth	1 mo	2 mos	4 mos	6 mos	12 mos	15 mos	18 mos	24 mos	4-6 yrs	11-12 yrs	14-18 yrs
Hepatitis B[2]	Hep B #1											
		Hep B #2			Hep B #3						Hep B[2]	
Diphtheria, Tetanus, Pertussis[3]			DTaP	DTaP	DTaP		DTaP[3]			DTaP	Td	
H. influenzae type b[4]			Hib	Hib	Hib	Hib						
Inactivated Polio[5]			IPV	IPV	IPV[5]					IPV[5]		
Pneumococcal Conjugate[6]			PCV	PCV	PCV	PCV						
Measles, Mumps, Rubella[7]						MMR				MMR[7]	MMR[7]	
Varicella[8]						Var					Var[8]	
Hepatitis A[9]									Hep A — in selected areas[9]			

Approved by the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP).

1. This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of 11/1/00, for children through 18 years of age. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and its other components are not contraindicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

2. Infants born to HBsAg-negative mothers should receive the 1st dose of hepatitis B (Hep B) vaccine by age 2 months. The 2nd dose should be at least one month after the 1st dose. The 3rd dose should be administered at least 4 months after the 1st dose and at least 2 months after the 2nd dose, but not before 6 months of age for infants.

   Infants born to HBsAg-positive mothers should receive hepatitis B vaccine and 0.5 mL hepatitis B immune globulin (HBIG) within 12 hours of birth at separate sites. The 2nd dose is recommended at 1-2 months of age and the 3rd dose at 6 months of age.

   Infants born to mothers whose HBsAg status is unknown should receive hepatitis B vaccine within 12 hours of birth. Maternal blood should be drawn at the time of delivery to determine the mother's HBsAg status; if the HBsAg test is positive, the infant should receive HBIG as soon as possible (no later than 1 week of age).

   All children and adolescents who have not been immunized against hepatitis B should begin the series during any visit. Special efforts should be made to immunize children who were born in or whose parents were born in areas of the world with moderate or high endemicity of hepatitis B virus infection.

3. The 4th dose of DTaP (diphtheria and tetanus toxoids and acellular pertussis vaccine) may be administered as early as 12 months of age, provided 6 months have elapsed since the 3rd dose and the child is unlikely to return at age 15-18 months. Td (tetanus and diphtheria toxoids) is recommended at 11-12 years of age if at least 5 years have elapsed since the last dose of DTP, DTaP or DT. Subsequent routine Td boosters are recommended every 10 years.

4. Three *Haemophilus influenzae* type b (Hib) conjugate vaccines are licensed for infant use. If PRP-OMP (PedvaxHIB® or ComVax® [Merck & Co., Inc.]) is administered at 2 and 4 months of age, a dose at 6 months is not required. Because clinical studies in infants have demonstrated that using some combination products may induce a lower immune response to the Hib vaccine component, DTaP/Hib combination products should not be used for primary immunization in infants at 2, 4 or 6 months of age, unless FDA-approved for these ages.

5. An all-IPV schedule is recommended for routine childhood polio vaccination in the United States. All children should receive four doses of IPV at 2 months, 4 months, 6-18 months, and 4-6 years of age. Oral polio vaccine (OPV) should be used only in selected circumstances.

6. The heptavalent conjugate pneumococcal vaccine (PCV) is recommended for all children 2-23 months of age. It also is recommended for certain children 24-59 months of age.

7. The 2nd dose of measles, mumps, and rubella (MMR) vaccine is recommended routinely at 4-6 years of age but may be administered during any visit, provided at least 4 weeks have elapsed since receipt of the 1st dose and that both doses are administered beginning at or after 12 months of age. Those who have not previously received the second dose should complete the schedule by the 11-12 year old visit.

8. Varicella (Var) vaccine is recommended at any visit on or after the first birthday for susceptible children, i.e. those who lack a reliable history of chickenpox (as judged by a health care provider) and who have not been immunized. Susceptible persons 13 years of age or older should receive 2 doses, given at least 4 weeks apart.

9. Hepatitis A (Hep A) is shaded to indicate its recommended use in selected states and/or regions, and for certain high risk groups; consult your local public health authority.

For additional information about the vaccines listed above, please visit the National Immunization Program Home Page at http://www.cdc.gov/nip/ or call the National Immunization Hotline at 800-232-2522 (English) or 800-232-0233 (Spanish).

Pertussis is common in developing countries and in other areas where pertussis immunization levels are low. Infants and children leaving the United States should be as well immunized as possible. Optimum protection against diphtheria, tetanus, and pertussis in the first year of life is achieved with three doses of diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP), the first administered when the infant is 6 to 8 weeks of age and the next two at 4- to 8-week intervals. A fourth dose of DTaP should be administered 6 to 12 months after the third dose when the infant is 15 to 18 months of age. A fifth (booster) dose is recommended when the child is 4 to 6 years of age. The fifth dose is not necessary if the fourth dose in the primary series was given after the child's fourth birthday. Two doses of DTaP received at intervals at least 4 weeks apart can provide some protection, particularly against diphtheria and tetanus; however, a single dose offers little protective benefit. Parents should be informed that infants and children who have not received at least three doses of DTaP might not be fully protected from pertussis. For infants and children younger than 7 years of age, if an accelerated schedule is required to complete the series prior to travel, the schedule may be started as soon as the infant is 6 weeks of age, with the second and third doses given 4 weeks after each preceding dose (see Table 1-3). The fourth dose should not be given before the infant is 12 months of age and should be separated from the third dose by at least 6 months. The fifth (booster) dose should not be given before the child is 4 years of age.

Measles Vaccine

Measles is an endemic disease in many developing countries and in other countries where measles immunization levels are low. Because the risk of contracting measles in many countries is greater than in the United States, infants and children should be as well protected as possible before leaving the United States. Infants and children who travel or live abroad should be vaccinated at an earlier age than is recommended for infants and children remaining in the United States. Before their departure from the United States, infants and children 12 months of age or older should have received two doses of measles, mumps, and rubella (MMR) vaccine separated by at least 28 days, with the first dose administered on or after the first birthday. Infants 6 through 11 months of age should receive a dose of monovalent measles vaccine before departure. If monovalent measles vaccine is not available, no specific contraindication exists to administering MMR to infants 6 through 11 months of age. However, because the risk for serious disease from either mumps or rubella infection among infants is relatively low and because infants younger than 12 months of age are less likely to develop serologic evidence of immunity when vaccinated with MMR antigens than are older infants and children, mumps and rubella vaccines generally are administered only to infants and children 12 months of age or older. Infants administered monovalent measles vaccine or MMR before their first birthday should be considered potentially susceptible to all three diseases and should be revaccinated with two doses of MMR, the first of which should be administered when the infant is 12 to 15 months of age (12 months if the infant remains in an area where disease risk is high) and the second at least 28 days later.

Parents who travel or reside abroad with infants younger than 12 months of age should have acceptable evidence of immunity to rubella and mumps, as well as measles, so they will not become infected if their infants contract these diseases. An infant younger than 6 months of age is usually

protected against measles, mumps, and rubella by maternally derived antibodies and ordinarily does not require additional protection unless his or her mother is diagnosed with measles.

Mumps and Rubella Vaccine(s)

Because the risk of serious disease from infection with either mumps or rubella in infants is low, mumps and rubella vaccine(s) generally should not be administered to infants younger than 12 months of age unless measles vaccine is indicated and single-antigen measles vaccine is not available. However, parents of an infant younger than 12 months of age should be immune to mumps and rubella so they will not expose the infant or become infected if the infant develops illness.

Varicella Vaccine

Varicella (chickenpox) is an endemic disease throughout the world. A single dose of varicella vaccine should be administered to all susceptible infants and children without contraindications at 12 months of age or older. Infants and children who have a reliable history of having had chickenpox do not need to be vaccinated. Infants younger than 12 months of age will generally be protected from varicella because of passive maternal antibody.

Polio Vaccine

Because OPV is no longer recommended for routine immunization in the United States, all infants and children should receive four doses of IPV at 2, 4, and 6 to 18 months and 4 to 6 years of age. If accelerated protection is needed, the minimum interval between doses should be 4 weeks, although the preferred interval between the second and third doses is 2 months. Infants and children who have initiated the poliovirus vaccination series with one or more doses of OPV should receive IPV to complete the series.

Haemophilus Influenzae Type b Conjugate Vaccine

Haemophilus influenzae type b (Hib) is an endemic disease worldwide. Risk of acquiring the disease might be higher in developing countries than in the United States. In the United States, four types of Hib conjugate vaccines are available, three of which may be used in infants beginning at 6 weeks of age. Two Hib conjugate vaccines for infants are also available as combined DTP–Hib vaccines. Routine Hib vaccination beginning at 2 months of age is recommended for all U.S. children. The first dose may be given when the infant is as young as 6 weeks of age. Hib vaccine should **never** be given to an infant younger than 6 weeks of age. A primary series consists of two or three doses (depending on the type of vaccine used) separated by 4 to 8 weeks. A booster dose is recommended when the infant is 12 to 15 months of age (see Chapter 3 "Specific Recommendations for Vaccinations and Disease Prevention," "*Haemophilus Influenzae* Type b Meningitis and Invasive Disease," pages 84 through 86).

If vaccination is started when the infant or child is 7 months of age or older, fewer doses may be required. If different brands of vaccine are administered, a total of three doses of Hib conjugate

vaccine completes the primary series. After completion of the primary infant vaccination series, any of the licensed Hib conjugate vaccines may be used for the booster dose when the infant is 12 to 15 months of age.

Infants and children should have optimal protection prior to travel. If previously unvaccinated, infants younger than 15 months of age should ideally receive at least two vaccine doses prior to travel. An interval as short as 4 weeks between these two doses is acceptable.

Unvaccinated infants and children 15 through 59 months of age should receive a single dose of Hib vaccine.

Hepatitis B Vaccine

Hepatitis B vaccine is recommended for all infants beginning either at birth or by 2 months of age. Infants and young children who have not previously been vaccinated and who are traveling to areas with intermediate and high hepatitis B virus (HBV) endemicity might be at risk if they are directly exposed to blood from the local population. Circumstances in which HBV transmission could occur include receipt of blood transfusions not screened for HBV surface antigen (HBsAg), exposure to unsterilized needles (or other medical or dental equipment) in local health facilities, or continuous close contact with local residents who have open skin lesions (impetigo, scabies, or scratched insect bites). Such exposures are most likely to occur if an infant or a child is living for long periods in smaller cities or rural areas and in close contact with the local population. Infants and children who will live in an area of intermediate or high HBV endemicity for at least 6 months and who are expected to have the preceding exposures should receive the three doses of HBV vaccine. The interval between doses one and two should be 1 to 2 months. Between doses two and three, the interval should be a minimum of 2 months; the third dose should not be given before the infant is 6 months of age. (See Table 1-2, for the suggested schedule and Table 3-7, for vaccine-specific doses.)

Other Vaccines and Immune Globulin

Typhoid Vaccine

Typhoid vaccination is not required for international travel. No data are available concerning the efficacy of typhoid vaccine in infants. Breast-feeding is likely to be protective against typhoid; careful preparation of formula and food from safe water and foodstuffs should protect non-breast-fed infants. Typhoid vaccine is recommended for children 2 years of age or older traveling to areas where there is a recognized risk of exposure to *Salmonella typhi*, particularly if they are traveling to highly endemic areas. (See Chapter 3 "Specific Recommendations for Vaccinations and Disease Prevention," "Typhoid Fever," pages 146 through 149, for information on dosage and route of administration of the vaccines.)

Table 1-4.—Recommended Immunization Schedule for People Older Than 7 Years of Age Not Vaccinated at the Recommended Time in Early Infancy.*

TIMING	VACCINES	COMMENTS
First visit	Tetanus and diphtheria toxoids†, IPV, MMR§, varicella, hepatitis B¶	Primary poliovirus vaccination is not routinely recommended for people 18 years of age or older, unless traveling to infected areas. Varicella vaccine is recommended for all susceptible people without contraindications older than 12 months of age. Infants and children 12 months through 12 years of age should receive one dose. Adolescents and adults 13 years of age or older should receive two doses separated by 4 to 8 weeks.
Second visit (4 to 8 weeks after first visit)	Tetanus and diphtheria toxoids, IPV, MMR**, varicella, hepatitis B¶	Adolescents and adults 13 years of age or older should receive two doses of varicella vaccine separated by 4 to 8 weeks. A second dose of MMR is recommended for international travelers.
Third visit (6 months after second visit)	Tetanus and diphtheria toxoids, IPV, Hepatitis B¶	The third dose of IPV may be given as soon as 4 weeks after the second dose. The third dose of hepatitis B vaccine may be given as soon as 2 months after the second dose and 4 months after the first dose.
Additional visits	Tetanus and diphtheria toxoids	Repeat every 10 years throughout life.

Abbreviated forms used in table: IPV - inactivated poliovirus; MMR - measles, mumps, and rubella.

*See individual Advisory Committee on Immunization Practices (ACIP) recommendations for details.

†The whole-cell pertussis (DTP) and acellular pertussis (DTaP) doses administered to children younger than 7 years of age who remain incompletely vaccinated at 7 years of age or older should be counted as prior exposure to tetanus and diphtheria toxoids, (for example, a child who previously received two doses of DTP needs only one dose of Td to complete a primary series for tetanus and diphtheria.

§People born before 1957 can generally be considered immune to measles, mumps, and rubella. Birth before 1957 should not be accepted as evidence of rubella immunity for women who might become pregnant.

¶Anyone younger than 18 years of age should receive a three-dose series of hepatitis B (HBV) vaccine. For anyone 18 years of age or older, high-risk groups for whom vaccination is recommended include people with occupational exposure risks, such as health care and public safety workers who have occupational exposure to blood, clients and staff of institutions for the developmentally disabled, hemodialysis patients, recipients of certain blood products (for example, clotting factor concentrates), household contacts and sex partners of HBV carriers, injecting drug users, sexually active homosexual and bisexual men, certain sexually active heterosexual men and women, inmates of long-term correctional facilities, certain international travelers, and families of HbsAg-positive adoptees from countries where HBV infection is endemic.

* *The ACIP recommends a second dose of measles-containing vaccine (MMR) for certain groups. Unvaccinated children should receive two doses of live measles-containing vaccine at least 4 weeks apart. In addition, the following people born in 1957 or later should have two doses of MMR or other evidence of measles immunity: (a) those entering post-high school educational settings, (b) those beginning employment in health care settings who will have direct patient contact, and (c) international travelers.

Table 1-5.—Minimum Age for Initial Vaccination and Minimum Interval Between Vaccine Doses, by Type of Vaccine.

VACCINE	MINIMUM AGE FOR FIRST DOSE*	MINIMUM INTERVAL FROM DOSE 1 TO 2*	MINIMUM INTERVAL FROM DOSE 2 TO 3*	MINIMUM INTERVAL FROM DOSE 3 TO 4*
DTaP or DT†	6 weeks	4 weeks	4 weeks	6 months
Hib (primary series)				
HbOC	6 weeks	4 weeks	4 weeks	§
PRP-T	6 weeks	4 weeks	4 weeks	§
PRP-OMP	6 weeks	4 weeks	§	
IPV	6 weeks	4 weeks	4 weeks	4 weeks¶
MMR	12 months	4 weeks		
Hepatitis B	Birth	4 weeks	8 weeks††	
Varicella	12 months**	4 weeks		
Pneumococcal conjugate vaccine	6 weeks	4 weeks	4 weeks	8 weeks§§

Abbreviated forms used in table: Hib - *Haemophilus influenzae* type b; IPV - inactivated poliovirus; MMR - measles, mumps, and rubella.

*These minimum acceptable ages and intervals might not correspond with the *optimal* recommended ages and intervals for vaccination. The childhood immunization schedule is published each January in the *Morbidity and Mortality Weekly Report*.

†Diphtheria and tetanus toxoids and acellular pertussis vaccine.

§The booster dose of Hib vaccine recommended following the primary vaccination series should be administered no earlier than 12 months of age and at least 8 weeks after the previous dose.

¶It is preferable to administer the fourth dose of the polio series 3 to 4 years after the third dose.

**Although the age for measles vaccination may be as young as 6 months in outbreak areas where cases are occurring in infants younger than 12 months of age, infants initially vaccinated before the first birthday should be revaccinated at 12 to 15 months of age and an additional dose of vaccine should be administered at the time of school entry or according to local policy. Doses of MMR or other measles-containing vaccines should be separated by at least 4 weeks.

††This final dose is recommended at least 4 months after the first dose and no earlier than 6 months of age.

§§The fourth (booster) dose should be no earlier than 12 months of age and at least 8 weeks after the previous dose.

Yellow Fever Vaccine

Because infants are at high risk of developing encephalitis from yellow fever vaccine, the recommendations for vaccinating infants should be considered on an individual basis. Although the incidence of these adverse events has not been clearly defined, 14 of 18 reported cases of post-vaccination encephalitis were in infants younger than 4 months of age. One fatal case confirmed by viral isolation was in a 4-year-old child. The ACIP and the World Health Organization recommend that yellow fever vaccine never be given to infants younger than 4 months of age. Yellow fever vaccine can be given to infants and children 9 months of age or older if they are traveling to or living in areas of South America and Africa where yellow fever infection is officially reported (see *Summary of Health Information for International Travel*, also known as the "Blue Sheet") or to countries that require yellow fever immunization (see Chapter 2 "Yellow Fever Vaccine Requirements and Information on Malaria Risk and Chloroquine Resistance, by Country," pages 23 through 54). Infants and children 9 months of age or older also should be immunized if they travel outside urban areas within the yellow fever endemic zone (see pages 23 through 54 and maps on pages 156 and 157). Infants 6 through 8 months of age should be vaccinated only if they travel to areas of ongoing epidemic yellow fever and a high level of protection against mosquito bites is not possible. Immunization of children 4 through 6 months of age should be considered only under unusual circumstances (consult the Centers for Disease Control and Prevention [CDC]), and in no instance should infants younger than 4 months of age receive yellow fever vaccine. Travelers with infants younger than 9 months of age should be strongly advised against traveling to areas with epidemic yellow fever.

Hepatitis A Vaccine or Immune Globulin for Hepatitis A

Infants and children traveling to developing countries are at increased risk of acquiring hepatitis A virus (HAV) infection, especially if their travel is outside usual tourist routes, if they will be eating food or drinking water in settings of questionable sanitation, or if they will be in contact with local residents in settings of poor sanitation (see Chapter 3 "Specific Recommendations for Vaccinations and Disease Prevention," "Hepatitis, Viral, Type A," pages 86 through 91). Although HAV is rarely severe in infants and children younger than 5 years of age, those infected efficiently transmit infection to other infants and children and to adults. Immune globulin (IG) should be given to infants younger than 2 years of age in the same schedule as that recommended for adults (Table 3-6). Children 2 years of age or older should receive the pediatric formulation of HAV vaccine (Tables 3-4 and 3-5) or IG (Table 3-6). The first dose of vaccine should be given at least 4 weeks prior to travel.

Other Diseases

See pages 106 through 120 and 173 and 174, respectively, for discussion of malaria and diarrhea in infants.

Chapter 2

Yellow Fever Vaccine Requirements and Information on Malaria Risk and Chloroquine Resistance, By Country

YELLOW FEVER VACCINE REQUIREMENTS AND INFORMATION ON MALARIA RISK AND CHLOROQUINE RESISTANCE, BY COUNTRY

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Afghanistan	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All, except no risk at altitudes higher than 2,000 meters (6,561 feet)	Confirmed
Albania	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Algeria	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	Malaria risk is limited to one small focus in Sahara region in Ihrir (Illizi Department). Prophylaxis is not recommended.	None
Andorra	Not required.	None	Not applicable
Anguilla (U.K.)	If traveling from an infected area (see the Blue Sheet or http://www.cdc.gov/travel/blusheet.htm) and older than 1 year of age.	None	Not applicable
Angola	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Antigua and Barbuda	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Argentina	Not required. Risk in northeastern forest areas only. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	Rural areas near Bolivian border (Salta and Jujuy provinces) and along the border with Paraguay (Misiones and Corrientes provinces)	None

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Armenia	Not required.	Risk limited to western border areas: Masis, Ararat, and Artashat regions in Ararat District	None
Australia **Note:** Australia is not bound by the International Health Regulations (see pages 3 and 4)	If traveling within 6 days of having stayed overnight in a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and if older than 1 year of age.	None	Not applicable
Austria	Not required.	None	Not applicable
Azerbaijan	Not required.	Rural lowlands, with highest risk in areas between Kura and Araks Rivers	None
Azores (Portugal)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. **Exception:** Not required if in transit at Santa Maria.	None	Not applicable
Bahamas, The	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Bahrain	Not required	None	Not applicable
Bangladesh	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Required also for travelers arriving from or transiting: **Africa:** Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo	All, except no risk in city of Dhaka	Widespread along northern and eastern borders with India and Burma (Myanmar) and in the southeastern part of the country

	(formerly, Zaire), Equatorial Guinea, Ethiopia, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Malawi, Mali, Mauritania, Niger, Nigeria, Rwanda, São Tomé and Principe, Senegal, Sierra Leone, Somalia, Sudan (south of 15° N), Tanzania (United Republic of), Togo, Uganda, and Zambia. **Americas:** Belize, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, French Guiana, Guatemala, Guyana, Honduras, Nicaragua, Panama, Peru, Suriname, and Venezuela. **Carribean:** Trinidad and Tobago. Any person (including infants) arriving by air or sea without a certificate within 6 days of departure from or transmit through an infected area will be isolated up to 6 days.		
Barbados	If traveling from an infected areas (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Belarus	Not required.	None	Not applicable
Belgium	Not required.	None	Not applicable
Belize	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All, except no risk in Belize City	None
Benin	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Bermuda (U.K.)	Not required.	None	Not applicable
Bhutan	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	Rural, in districts bordering India	Confirmed

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Bolivia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Bolivia recommends vaccination for travelers who are destined for risk areas, such as the departments of Beni, Cochabamba, Santa Cruz, and the subtropical part of La Paz Department. However, CDC recommends vaccination for all travelers (from any country) older than 9 months of age.	Risk in areas below 2,500 meters (8,202 feet) in the following departments: Beni, Chuquisaca, Cochabamba, La Paz, Pando, Santa Cruz, and Tarija	Confirmed
Bosnia and Herzegovina	Not required.	None	Not applicable
Botswana	Not required.	Northern part of country (north of 21° S)	Confirmed
Brazil	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 9 months of age, unless the traveler has a waiver stating that immunization is contraindicated on medical grounds. However, CDC recommends for all travelers (from any country) older than 9 months of age who travel outside urban areas. Also required for travelers arriving from: **Africa:** Angola, Cameroon, Democratic Republic of Congo (formerly Zaire), Gabon, Gambia, Ghana, Guinea, Liberia, Nigeria, Sierra Leone, and Sudan. **Americas:** Bolivia, Ecuador, Colombia, and Peru. Brazil recommends vaccination for travel to rural areas in: Acre, Amapá, Amazonas, Goiás, Maranhaõ, Mato Grosso, Mato Grosso do Sul, Pará, Rondônia, Roraima, and Tocantins, as well as certain areas of Minas Gerais, Paraná, and São Paulo.	States of Acre, Rondônia, Amapá, Amazonas, Roraima, and Tocantins. Parts of states of Maranhaõ (western part), Mato Grosso (northern part), and Pará (except Belem City). There is also transmission in urban areas, including large cities such as Porto Velho, Boa Vista, Macapa, Manaus, Santarem, and Maraba.	Confirmed

Brunei	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. **Note:** Required also for travelers coming from or transiting endemic zones within the preceding 6 days (see pages 156 and 157).	None	Not applicable
Bulgaria	Not required.	None	Not applicable
Burkina Faso	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Burma (Myanmar)	If traveling from an infected are (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Required also for nationals and residents of Burma departing for an infected area.	Rural only. No risk in cities of Rangoon (Yangon) and Mandalay	Confirmed
Burundi	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Cambodia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All, except no risk in Phnom Penh. There is malaria risk at the temple complex at Angkor Wat.	Confirmed
Cameroon	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Canada	Not required.	None	Not applicable
Canary Islands (Spain)	Not required.	None	Not applicable

Cape Verde	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also if coming from countries having reported cases in the last 6 years.	Limited risk on the island of Saõ Tiago only	None
Country	**Yellow Fever Vaccination**	**Malaria**	
		Area of Risk	**Chloroquine Resistance**
Cayman Islands (U.K.)	Not required.	None	Not applicable
Central African Republic	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Chad	Not required; however, Chad recommends vaccination for all travelers older than 1 year of age. CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Chile	Not required.	None	Not applicable
China	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	Rural areas only of the following provinces: Hainan, Yunnan, Fuijan, Guangdong, Guangxi, Guizhou, Sichuan, Xizang (in the Zangbo River valley only), Anhui, Hubei, Hunan, Jiangsu, Jiangxi, Shandong, Shanghai, and Zhejiang. In provinces with risk, transmission occurs only during warm weather: north of latitude 33° N, July–November; between latitude 25° N and 33° N, May–December; south of latitude 25° N, transmission occurs year-round. Travelers to cities and popular tourist areas, including Yangtze River cruises, are not at risk and do not need to take chemoprophylaxis.	Confirmed in the provinces of Hainin, Yunnan, and Guangxi. Other provinces do not have chloroquine-resistant malaria

Christmas Island (Australia) **Note:** Christmas Island is not bound by the International Health Regulations (see page 3 and 4)	If traveling within 6 days of having stayed overnight or longer in a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and if older than 1 year of age.	None	Not applicable
Colombia	Not required; however, Colombia recommends vaccination for travelers to middle valley of the Magdelena River; eastern and western foothills of the Cordillera Oriental from the border with Ecuador to that with Venezuela; Urabá, the foothills of the Sierra Nevada; the eastern plains (Orinoquia); and Amazonia. CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	Risk in all rural areas, except no risk at altitudes higher than 800 meters (2,624 feet). No risk in Bogota and vicinity. No risk on Carribean coast.	Confirmed
Comoros	Not required.	All	Confirmed
Congo	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Cook Islands (New Zealand)	Not required.	None	Not applicable
Costa Rica	Not required.	Provinces of Alajuela, Limon, Guanacaste, and Heredia. No risk in Limon City.	None
Côte d'Ivoire (formerly Ivory Coast)	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Croatia	Not required.	None	Not applicable
Cuba	Not required.	None	Not applicable
Cyprus	Not required.	None	Not applicable
Czech Republic	Not required.	None	Not applicable

Democratic Republic of the Congo (formerly Zaire)	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Denmark	Not required.	None	Not applicable
Djibouti	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	All	Confirmed

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Dominica	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Dominican Republic	Not required.	Rural, except no risk in tourist resorts; highest risk in provinces bordering Haiti.	None
Ecuador	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas. Travelers to the Galápagos Islands who also make intermediate stops in rural areas might be at risk and should obtain yellow fever immunization.	Risk in all areas, except no risk at altitudes higher than 1,500 meters (4,921 feet). No risk in the cities of Guayaquil and Quito, the central highland tourist areas, and the Galápagos Islands.	Confirmed
Egypt	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Also required if arriving from or transiting: **Africa:** Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Ethiopia, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Mali, Niger, Nigeria, Rwanda, São Tomé and Principe, Senegal, Sierra Leone, Somalia, Sudan (south of latitude 15° N), Tanzania, Togo, Uganda, and Zambia. **Americas:** Belize, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, French Guiana, Guyana, Panama, Peru, Suriname, and Venezuela. **Carribean:** Trinidad and Tobago.	Very limited risk in El Faiyûm area only. Prophylaxis is not recommended. **Note:** Travelers visiting tourist areas, including Nile River cruises, are not at risk and need no prophylaxis.	None

	Air passengers in transit but coming from these countries or areas without a certificate will be detained in the precincts of the airport until they resume their journey. All travelers arriving from Sudan are required to possess a vaccination or location certificate issued by a Sudanese official center stating that they have not been in Sudan south of latitude 15° N within the preceding 6 days.		
El Salvador	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm. or the Blue Sheet) and older than 6 months of age.	Rural areas of the departments of Santa Ana, Ahuachapán, and La Unión	None
Equatorial Guinea	If traveling form an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Eritrea	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All, except no risk at altitudes higher than 2,200 meters (7,218 feet). No risk in Asmara.	Confirmed
Estonia	Not required.	None	Not applicable
Ethiopia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All, except no risk in Addis Ababa and at altitudes higher than 2,000 meters (6,561 feet)	Confirmed
Falkland Islands (U.K.)	Not required.	None	Not applicable
Faroe Islands (Denmark)	Not required.	None	Not applicable

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Fiji	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age, within 10 days of having stayed overnight or longer in an infected area.	None	Not applicable
Finland	Not required.	None	Not applicable
France	Not required.	None	Not applicable
French Guiana	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
French Polynesia, includes the island groups of: Society Islands (Tahiti, Mooréa, and Bora-Bora); Marquesas Islands (Hiva Oa and Ua Huka); and Austral Islands (Tubuai and Rurutu)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Gabon	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Gambia, The	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (pages 156 and 157). CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed

Georgia	Not required.	Southeastern part of the country, in the Kakheti and Kveno Kartli regions	None
Germany	Not required.	None	Not applicable
Ghana	Required upon arrival from all countries.	All	Confirmed
Gibraltar (U.K.)	Not required.	None	Not applicable
Greece	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 6 months of age.	None	Not applicable
Greenland (Denmark)	Not required.	None	Not applicable
Grenada	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Guadeloupe (France)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Guam (U.S.)	Not required.	None	Not applicable
Guatemala	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	Rural only, except no risk at altitudes higher than 1,500 meters (4,921 feet) No risk in Antigua or Lake Atitian	None
Guinea	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed

Guinea-Bissau	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
	Required also for travelers arriving from: **Africa:** Angola, Benin, Burkina Faso, Burundi, Cape Verde, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of Congo, Djibouti, Equatorial Guinea, Ethiopia, Gabon, The Gambia, Ghana, Guinea, Kenya, Liberia, Madagascar, Mali, Mauritania, Mozambique, Niger, Nigeria, Rwanda, São Tomé and Principe, Senegal, Sierra Leone, Somalia, Tanzania (United Republic of), Togo, Uganda, and Zambia. **Americas:** Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Panama, Peru, Suriname, and Venezuela.		
Guyana	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas. Required also for travelers arriving from: **Africa:** Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Mali, Niger, Nigeria, Rwanda, São Tomé and Principe, Senegal, Sierra Leone, Somalia, Tanzania (United Republic of), Togo, and Uganda. **Americas:** Belize, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, French Guiana, Guatemala, Honduras, Nicaragua, Panama, Peru, Suriname, and Venezuela.	Risk in all areas of the interior; sporadic cases have also been reported along the coastal region.	Confirmed
Haiti	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All	None

Honduras	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	Rural only, including Roatán and other Bay Islands	None
Hungary	Not required.	None	Not applicable
Iceland	Not required.	None	Not applicable
India	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Required also for travelers arriving from or transiting: **Africa:** Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Ethiopia, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Mali, Niger, Nigeria, Rwanda, São Tomé and Principe, Senegal, Sierra Leone, Somalia, Sudan, Tanzania, Togo, Uganda, and Zambia. **Americas:** Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Panama, Peru, Suriname, and Venezuela. **Caribbean:** Trinidad and Tobago. Any person (except infants up to the age of 6 months) arriving without a certificate within 6 days of departure from or transit through an infected area will be isolated for up to 6 days.	All areas, including the cities of Delhi and Bombay, except no risk at altitudes higher than 2,000 meters (6,561 feet) in Himachal Pradesh, Jammu, Kashmir, and Sikkim	Confirmed
Indonesia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157).	Rural only, except high risk in all areas of Irian Jaya (Papua) (western half of the island of New Guinea). No risk in cities of Java and Sumatra and no risk for the main resort areas of Java and Bali. There is malaria risk at the temple complex of Borobudur.	Confirmed

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Iran	Not required.	Rural only in the provinces of Sistan-Baluchestan, the tropical part of Kerman, Hormozgan, parts of Bushehr, Fars, Ilam, Kohgiluyeh-Boyar, Lorestan, Chahar Mahal-Bakhtiari, and the north of Khuzestan	Confirmed
Iraq	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All of northern region; Duhok, Erbil, Ninawa, Sulaimaniya, Támim, and Basrah provinces	None
Ireland	Not required.	None	Not applicable
Israel	Not required.	None	Not applicable
Italy	Not required.	None	Not applicable
Jamaica	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Japan	Not required.	None	Not applicable
Jordan	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Kazakhstan	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	None	Not applicable
Kenya	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All (including game parks), except no risk in Nairobi and at altitudes higher than 2,500 meters (8,202 feet)	Confirmed

Kiribati (formerly Gilbert Islands), includes the islands: Tarawa, Tabuaeran (Fanning Island), and Banaba (Ocean Island)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Korea, North	Not required.	Limited malaria risk in some southern areas	None
Korea, South	Not required.	Risk limited to demilitarized zone (DMZ) and to rural areas in the northern parts of Kyonggi and Kangwon provinces	None
Kuwait	Not required	None	Not applicable
Kyrgyzstan	Not required.	None	Not applicable
Laos	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All, except no risk in city of Vientiane	Confirmed
Latvia	Not required.	None	Not applicable
Lebanon	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	None	Not applicable
Lesotho	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	None	Not applicable
Liberia	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Libya	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	None	Not applicable
Liechtenstein	Not required.	None	Not applicable
Lithuania	Not required.	None	Not applicable

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Luxembourg	Not required.	None	Not applicable
Macedonia, The Former Republic of	Not required.	None	Not applicable
Madagascar	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet); includes travelers in transit.	All	Confirmed
Madeira (Portugal)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. **Exception:** Not required for travelers in transit at Funchal and Porto Santo.	None	Not applicable
Malawi	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All	Confirmed
Malaysia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157).	Peninsular Malaysia and Sarawak (NW Borneo): malaria limited to remote areas. Urban and coastal areas: malaria free. Sabah (NE Borneo): malaria throughout. **Note:** Malaria transmission in Malaysia (except Sabah) is largely confined to rural areas not visited by most travelers; most travel to rural areas is during daytime hours when the risk of exposure is minimal.	Confirmed
Maldives	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	None	Not applicable
Mali	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed

Malta	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 9 months of age. Children younger than 9 months of age arriving from an infected area may be subject to isolation or surveillance.	None	Not applicable
Marshall Islands	Not required.	None	Not applicable
Martinique (France)	Not required.	None	Not applicable
Mauritania	Required upon arrival from all countries if traveler is older than 1 year of age. **Exception:** Not required for travelers from a noninfected area who stay less than 2 weeks.	All, except no risk in the northern areas of Dakhlet-Nouadhibou and Tiris-Zemour	Probable
Mauritius	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157)	Rural only, except no risk on Rodrigues Island	None
Mayotte (French territorial collectivity)	Not required.	All	Confirmed
Mexico	Not required.	Risk in rural areas, including resorts in rural areas of the following states: Campeche, Chiapas, Guerrero, Michoahan, Nayarit, Oaxaca, Quintana Roo, Sinaloa, and Tabasco. In addition, risk exists in the state of Jalisco (in its mountainous northern area only). Risk also exists in an area between 24° N and 28°N latitude, and 106° W and 110° W longitude. This area, which is rarely visited by tourists, includes parts of the states of Sonora, Chihuahua, and Durango. No malaria risk exists along the United States–Mexico border. No malaria risk exists in the major resorts along the Pacific and Gulf coasts.	None

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Micronesia (Federated States of), includes: Yap Islands, Pohnpei, Chuuk, and Kosrae	Not required.	None	Not applicable
Moldova	Not required.	None	Not applicable
Monaco	Not required.	None	Not applicable
Mongolia	Not required.	None	Not applicable
Montserrat (U.K.)	Not required.	None	Not applicable
Morocco	Not required.	Limited risk in rural areas of Khouribga Province. Prophylaxis is not recommended. The cities of Tangier, Rabat, Casablanca, Marrakech, and Fez do not have risk.	None
Mozambique	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	All	Confirmed
Namibia	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157) and for travelers on unscheduled flights who have transited an infected area. Children younger than 1 year of age might be subject to surveillance.	Risk in the northern regions and in Omaheke and Otjozondjupa and along the Kavango and Kunene rivers	Confirmed
Nauru	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable

Nepal	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	Rural areas in the Terai and Hill districts. No risk at altitudes higher than 1,200 meters (3,937 feet). No risk in Kathmandu on typical Himalayan treks .	Confirmed
Netherlands	Not required.	None	Not applicable
Netherlands Antilles	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 6 months of age.	None	Not applicable
New Caledonia (France)	If traveling from an infected area (see the Blue Sheet or http://www.cdc.gov/travel/blusheet.htm) and older than 1 year of age. **Note:** Cholera— not required; however, travelers from infected areas are required to complete a form for the Health Service.	None	Not applicable
New Zealand	Not required.	None	Not applicable
Nicaragua	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	Rural only; however, risk exists in outskirts of Managua	None
Niger	Required upon arrival from all countries if traveler is older than 1 year of age. Niger also recommends vaccination for travelers leaving the country.	All	Confirmed
Nigeria	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age.	All	Confirmed
Niue (New Zealand)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Northern Mariana Islands, includes: Saipan, Tinian, and Rota Island	Not required.	None	Not applicable

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Norway	Not required.	None	Not applicable
Oman	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet)	Limited risk in remote areas of Musandam Province	Confirmed
Pacific Islands, U.S. Trust Territory, includes: Johnston Atoll, Wake Island, and Midway Islands	Not required.	None	Not applicable
Pakistan	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157). Not required for infants younger than 6 months of age if the mother's certificate shows she was vaccinated before the child's birth.	Risk in all areas, including the cities; except, no risk at altitudes higher than 2,000 meters (6,562 feet)	Confirmed
Palau	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Panama	Not required, but Panama recommends for all travelers who are destined for Chepo, Darien, or San Blas. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	Risk exists in rural areas of three provinces: Bocas Del Toro, Darien, and San Blas. No risk in Panama City or in the former Canal Zone.	Confirmed in Darien and San Blas provinces, including San Blas Islands
Papua New Guinea	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	All	Confirmed

Paraguay	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas. Required also for travelers going to or coming from endemic zones (see pages 156 and 157).	Risk in three departments: Alto Paraná, Caaguazú, and Canendiyú	None
Peru	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 6 months of age. Peru recommends for those who intend to visit any jungle areas of the country below 2,300 meters (7546 feet). CDC also recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	Risk in all departments, except: Arequipa, Moquegua, Puno, and Tacna. No risk in cities. Travelers who will visit only Lima and its vicinity, coastal areas south of Lima, or the highland tourist areas (Cuzco, Machu Picchu, and Lake Titicaca) are not at risk and need no prophylaxis.	Confirmed
Philippines	If traveling form an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	Rural only, except no risk in provinces of Bohol, Catanduanes, and Cebu, and metropolitan Manila. **Note:** Malaria transmission in the Philippines is largely confined to rural areas not visited by most travelers; most travel to rural areas in the Philippines is during daytime hours when the risk of exposure is minimal.	Confirmed on islands of Basilian, Luzon, Mindanao, Mindoro, Palawan, and Sulu Archipelago
Pitcairn Islands (U.K.)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Poland	Not required.	None	Not applicable
Portugal	Required only for travelers older than 1 year of age arriving from infected areas and destined for the Azores and Madeira. However, no certificate is required for passengers in transit at Funchal, Porto Santo, and Santa Maria.	None	Not applicable
Puerto Rico (U.S.)	Not required.	None	Not applicable

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Qatar	Not required.	None	Not applicable
Réunion (France)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Romania	Not required.	None	Not applicable
Russia	Not required.	None	Not applicable
Rwanda	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Saint Helena (U.K.)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Saint Kitts (Saint Christopher) and Nevis (U.K.)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Saint Lucia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Saint Pierre and Miquelon (France)	Not required.	None	Not applicable
Saint Vincent and the Grenadines	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Samoa (formerly Western Samoa)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Samoa, American (U.S.)	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable

San Marino	Not required.	None	Not applicable
São Tomé and Principe	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed
Saudi Arabia	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet)	All of western provinces, except no risk in the high-altitude areas of Asir Province (Yemen border) and the urban areas of Jeddah, Mecca, Medina, and Taif.	Confirmed
Senegal	Required upon arrival from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Seychelles	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. A certificate is also required from travelers who have, within the preceding 6 days, transited an endemic area (see pages 156 and 157).	None	Not applicable
Sierra Leone	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Singapore	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from or transiting countries in the endemic zones (see pages 156 and 157).	None	Not applicable

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Slovakia	Not required.	None	Not applicable
Slovenia	Not required.	None	Not applicable
Solomon Islands	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All	Confirmed
Somalia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). Because of the lack of current surveillance information, CDC recommends for all travelers (from any country) older than 9 months of age.	All	Confirmed
South Africa	If traveling from a country any part of which is infected (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157).	Risk exists in the low altitude areas of the Mpumalanga Province (including Kruger National Park), Northern Province, and northeastern KwaZulu-Natal as far south as the Tugela River.	Confirmed
Spain	Not required.	None	Not applicable
Sri Lanka	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	Risk in all areas, except no risk in the districts of Colombo, Kalutara, and Nuwara Eliya	Confirmed
Sudan	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas. Might be required for travelers leaving Sudan.	All	Confirmed

Suriname	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	Rural only, except no risk in Paramaribo District and coastal areas north of latitude 5° N.	Confirmed
Swaziland	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet)	All lowlands	Confirmed
Sweden	Not required.	None	Not applicable
Switzerland	Not required.	None	Not applicable
Syria	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	Risk along the northern border, especially in the northeast part of the country.	None
Tajikistan	Not required.	Southern border; some central (Dushanbe), western (GornoBadakhshan), and northern (Leninabad) areas	Suspected
Tanzania	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157). Risk in northwestern forest areas only. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All, except no risk at altitudes higher than 1,800 meters (5,906 feet)	Confirmed
Thailand	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157).	Limited risk in the areas that border Cambodia, Laos, and Burma (Myanmar). No risk in cities and no risk in major tourist resorts. No risk in Bangkok, Chiang Mai, Chiang Rai, Pattaya, Phuket Island, and Ko Samui.	Confirmed
Togo	Required upon arrival from all countries if traveler is older than 1 year of age.	All	Confirmed

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Tokelau (New Zealand)	Not required.	None	Not applicable
Tonga	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Trinidad and Tobago	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	None	Not applicable
Tunisia	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	None	Not applicable
Turkey	Not required.	Southeast part of the country; Cukurova/ Amikova areas, except no risk on the Incerlik U.S. Air Force base. No risk on typical cruise itineries.	None
Turkmenistan	Not required.	Risk in some villages in the Mary, Lebap, and Balkan districts	None
Tuvalu	Not required.	None	Not applicable
Uganda	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age. Required also for travelers arriving from countries in the endemic zones (see pages 156 and 157). However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Ukraine	Not required.	None	Not applicable

United Arab Emirates	Not required.	Very limited risk in the foothill areas and valleys in the mountainous regions of the northern emirates bordering Oman's Musandam Province. No risk in Abu Dhabi or in the cities of Ajman, Dubai, Sharjah, or Umm al Qaiwan.	Confirmed
United Kingdom (with Channel Islands and Isle of Man)	Not required.	None	Not applicable
United States	Not required.	None	Not applicable
Uruguay	Not required.	None	Not applicable
Uzbekistan	Not required.	None	Not applicable
Vanuatu	Not required.	All	Confirmed
Venezuela	Not required. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	Risk exists in rural areas of the following states: Apure, Amazonas, Barinas, Bolivar, Sucre, Tachira, and Delta Amacuro.	Confirmed
Vietnam	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	Rural only, except no risk in the Red River delta and the coastal plain north of the Nha Trang.	Confirmed
Virgin Islands, U.K.	Not required.	None	Not applicable
Virgin Islands, U.S.	Not required.	None	Not applicable
Wake Island, U.S.	Not required.	None	Not applicable
Yemen	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet) and older than 1 year of age.	All, except no risk in altitudes above 2,000 meters (6,561 feet). No risk in Sana'a.	Confirmed
Yugoslavia	Not required.	None	Not applicable

Country	Yellow Fever Vaccination	Malaria	
		Area of Risk	Chloroquine Resistance
Zambia	Not required. Risk in western areas only. However, CDC recommends for all travelers (from any country) older than 9 months of age who go outside urban areas.	All	Confirmed
Zimbabwe	If traveling from an infected area (see http://www.cdc.gov/travel/blusheet.htm or the Blue Sheet).	All, except no risk in cities of Harare and Bulawayo	Confirmed

NOTES

CHAPTER 3
SPECIFIC RECOMMENDATIONS FOR VACCINATIONS AND DISEASE PREVENTION

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

Description

AIDS is a serious disease, first recognized as a distinct syndrome in 1981. This syndrome represents the late clinical state of infection with the human immunodeficiency virus (HIV), resulting in progressive damage to the immune system and in life-threatening infectious and noninfectious complications.

Occurrence

AIDS and HIV infection occur worldwide. Comprehensive surveillance systems are lacking in many countries, so the true number of cases is likely to be far greater than the numbers officially reported, particularly from developing nations. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 34.3 million people are HIV-infected worldwide. Because HIV infection and AIDS are globally distributed, the risk to international travelers is determined less by their geographic destination than by their sexual and drug-using behaviors.

Risk for Travelers

The risk of HIV infection for international travelers is generally low. Factors to consider when assessing risk include the extent of direct contact with blood or secretions and of sexual contact with potentially infected people. In addition, the blood supply in developing countries might not be adequately screened.

Preventive Measures

No vaccine is available to prevent infection with HIV. For information on the safety of vaccines for HIV-infected people, see Chapter 6, "Advising the Traveler With Special Needs," "Vaccine Recommendations for Travelers With Altered Immunocompetence, Including HIV," pages 209 through 211.

Travelers should be advised that HIV infection is preventable. HIV is transmitted through sexual intercourse and needle- or syringe-sharing; by medical use of blood, blood components, or organ or tissue transplantation; and perinatally from an infected woman to her infant. HIV is not transmitted through casual contact; air, food, or water routes; contact with inanimate objects; or mosquitoes or other arthropod vectors. The use of any public conveyance (for example, an airplane, an automobile, a boat, a bus, or a train) by people with AIDS or HIV infection does not pose a risk of infection for the crew members or other travelers.

Travelers should be advised that they are at risk if they:

- Have sexual intercourse (heterosexual or homosexual) with an infected person.

- Use or allow the use of contaminated, unsterilized syringes or needles for any injections or other skin-piercing procedures, including acupuncture, use of illicit drugs, steroid or vitamin injections, medical or dental procedures, ear or body piercing, or tattooing.

- Use infected blood, blood components, or clotting factor concentrates. HIV infection by this route is rare in those countries or cities where donated blood and plasma are screened for HIV antibody.

Travelers should be advised to avoid sexual encounters with people who are infected with HIV or whose HIV infection status is unknown. This includes avoiding sexual activity with intravenous drug users and people with multiple sexual partners, such as male or female sex workers. Condoms, when used consistently and correctly, prevent transmission of HIV. Travelers who engage in vaginal, anal, or oral-genital intercourse with anyone who is infected with HIV or whose infection status is unknown should use a latex condom. For those who are sensitive to latex, polyurethane or other plastic condoms are available. (Travelers should be advised to look for the words "for the prevention of disease" on the condom packaging.)

In many countries, needle sharing by intravenous drug users is a major source of HIV transmission and other infections, such as hepatitis B (HBV) and hepatitis C (HCV). Travelers should be advised not to use drugs intravenously or share needles for any purpose.

In the United States, Australia, New Zealand, Canada, Japan, and western European countries, the risk of transfusion-associated HIV infection has been virtually eliminated through required testing of all donated blood for antibody to HIV. In the United States, donations of blood and plasma must be screened for HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen.

If produced in the United States according to U.S. Food and Drug Administration-approved procedures, immune globulin preparations (such as those used for the prevention of hepatitis A (HAV) and HBV) and HBV vaccines undergo processes that are known to inactivate HIV; therefore, these products should be used as indicated. Less developed nations might not have a formal program for testing blood or biological products for antibody to HIV. In those countries, travelers should (when medically prudent) avoid use of unscreened blood-clotting factor concentrates or those of uncertain purity. If transfusion is necessary, the blood should be tested, if at all possible, for HIV antibody by appropriately trained laboratory technicians using a reliable test. (See Chapter 4, "Health Hints for the International Traveler," "WHO Blood Transfusion Guidelines for International Travelers," pages 185 and 186, for additional information.)

Needles used to draw blood or administer injections should be sterile, preferably single use and disposable, and prepackaged in a sealed container. Travelers with insulin-dependent diabetes or hemophilia, or who require routine or frequent injections should be advised to carry a supply of syringes, needles, and disinfectant swabs (for example, alcohol wipes) sufficient to last their entire stay abroad.

International travelers should be advised that some countries serologically screen incoming travelers (primarily those planning extended visits, such as for work or study) and deny entry to people with AIDS and those whose test results indicate infection with HIV. People intending to visit a country for a substantial period or to work or study abroad should be informed of the policies and requirements of the particular country. This information is usually available from the consular officials of the individual nations. An unofficial list that has been compiled by the U.S. Department of State can be found at the following Internet address: http://travel.state.gov/HIVtestingreqs.html.

Further information is available from 1-800-342-AIDS, toll free from the United States or its territories (for Spanish-speaking callers, 1-800-344-SIDA, or for hearing-impaired callers with teletype equipment, 1-800-AIDS-TTY).

AFRICAN SLEEPING SICKNESS (AFRICAN TRYPANOSOMIASIS)

Description

Trypanosomiasis is a systemic disease cause by the parasite *Trypanosoma brucei*. It is transmitted by the bite of the tsetse fly, a gray-brown insect about the size of the honeybee. Signs and symptoms are initially nonspecific (fever, skin lesions, rash, edema, or lymphadenopathy); however, the infection progresses to meningoencephalitis. Symptoms generally appear within 1 to 4 weeks of infection. East African trypanosomiasis (caused by *T. b. rhodesiense*) is more acute clinically than the West African form of the disease (caused by *T. b. gambiense*), and central nervous system involvement occurs earlier.

Occurrence

African trypanosomiasis is confined to tropical Africa between 15° north latitude and 20° south latitude, or from north of South Africa to south of Algeria, Libya, and Egypt.

Risk for Travelers

Tsetse flies inhabit rural areas only, living in the woodland and thickets of the savannah and the dense vegetation along streams. Although infection of international travelers is rare, cases have occurred and travelers visiting game parks and remote areas should be advised to take precautions. Travelers to urban areas are not at risk.

Preventive Measures

No vaccine is available to prevent this disease. Tsetse flies are attracted to moving vehicles and dark, contrasting colors. They are not affected by insect repellents and can bite through lightweight

clothing. Areas of heavy infestation tend to be sporadically distributed and are usually well known to local inhabitants. Avoidance of such areas is the best means of protection. Travelers at risk should be advised to wear clothing of wrist and ankle length that is made of medium-weight fabric in neutral colors that blend with the background environment.

Treatment

Travelers who sustain tsetse fly bites and develop high fever or other manifestations of African trypanosomiasis should be advised to seek early medical attention. The infection can usually be cured by an appropriate course of anti-trypanosomal therapy. Travelers should be advised to consult an infectious disease or tropical medicine specialist.

AMEBIASIS

Description

Amebiasis is caused by the protozoan parasite *Entamoeba histolytica*. Infection is acquired by the fecal-oral route, either by person-to-person contact or indirectly by eating or drinking fecally contaminated food or water. The clinical spectrum of intestinal amebiasis ranges from asymptomatic infection to fulminant colitis. *Entamoeba dispar*, which is nonpathogenic, cannot be distinguished from the pathogen *E. histolytica* by routine diagnostic methods. In people infected with *E. histolytica* who are symptomatic, the most common symptom is diarrhea. The diarrhea can evolve to painful, bloody bowel movements, with or without fever (amebic dysentery). Occasionally, amebiasis causes disease outside the intestines, most notably in the liver (amebic liver abscess).

Occurrence

Amebiasis occurs worldwide, especially in regions with poor sanitation.

Risk for Travelers

For travelers to developing countries, risk for infection is highest for those who live in or visit rural areas, spend time in back country areas, or eat or drink in settings of poor sanitation.

Preventive Measures

No vaccine is available. Travelers to developing countries should be advised to follow the precautions detailed in Chapter 4, “Health Hints for the International Traveler,” “Risks From Food and Drink,” pages 165 through 168.

Treatment

Specific treatment is available and travelers should be advised to consult an infectious disease or tropical medicine specialist.

BOVINE SPONGIFORM ENCEPHALOPATHY AND NEW VARIANT CREUTZFELDT-JAKOB DISEASE

Description

Since 1996, evidence has been increasing for a causal relationship between ongoing outbreaks in Europe of a disease in cattle called bovine spongiform encephalopathy (BSE, or "mad cow disease") and a disease in humans called new variant Cruetzfeldt-Jakob disease (nvCJD). Both disorders are invariably fatal brain diseases with unusually long incubation periods measured in years, and are caused by an unconventional transmissible agent (a prion). Although there is strong evidence that the agent responsible for these human cases was the same agent responsible for the BSE outbreaks in cattle, the specific foods that might be associated with the transmission of the agent from cattle to humans are unknown. However, bioassays have identified the presence of the BSE agent in the brain, spinal cord, retina, dorsal root ganglia (nervous tissue located near the backbone), distal ileum, and bone marrow of cattle experimentally infected with this agent by the oral route.

In addition to cattle, sheep are susceptible to experimental infection with the BSE agent by the oral route. Thus, in countries where flocks of sheep and goats might have been exposed to the BSE agent through contaminated feed, a theoretical risk exists that these animals might have developed infections caused by the BSE agent and that these infections are being maintained in the flocks, even in the absence of continued exposure to contaminated feed (for example, through maternal transmission). In December 1999, the World Health Organization published a report encouraging countries to conduct risk assessments related to BSE in populations of sheep and goats. In August 2000, survey data of sheep farms in the United Kingdom were reported to have shown no rise in BSE-like illnesses in sheep that could be related to the BSE outbreaks in cattle. Currently, cattle remain the only known food animal species with disease caused by the BSE agent.

Occurrence

From 1986 through August 2000, >99% of the cases of BSE reported were from the United Kingdom, but endemic cases of BSE were also reported in other European countries, including Belgium, Denmark, France, Liechtenstein, Luxembourg, Netherlands, Portugal, Ireland, and Switzerland. From 1995 through early August 2000, 79 human cases of nvCJD were reported in the United Kingdom, 3 in France, and 1 in Ireland. During that period, the reported rate of occurrence of these new cases increased. Based on data available in mid-2000, the proportion of the total number of BSE cases in Europe reported outside the United Kingdom rose to 6.7% in 1998 and to >10% in 1999, primarily reflecting the declining large outbreak of BSE in the United Kingdom and the sharp

rise in the number of reported cases in Portugal. In July 2000, the European Union Scientific Steering Committee (SSC) on the geographic risk of BSE adopted a final opinion on the risk of BSE in the cattle populations of 23 different countries. The United Kingdom and Portugal were the only ones classified as countries where BSE was confirmed in domestic cattle at a higher level (over 100 cases per 1 million adult cattle in the 12-month period ended June 15, 2000). Despite the absence of reported endemic cases of BSE in Germany, Italy, and Spain, the SSC concluded that it was likely that cattle were infected in those three countries and classified their geographic risk of BSE as similar to that of the countries where BSE had been confirmed (but at a level below 100 cases per 1 million adult cattle). Because no data were available from Greece, the SSC reported that it was prudent to assume that the geographic BSE risk there was at a "high level." The reports of the final opinion of the SSC and its BSE risk assessments of individual countries are available on the European Union Commission on Food Safety and Animal Welfare Internet website, http://europa.eu.int/comm/food/index_en.html (search for "BSE-risk assessment"). In addition, the numbers of reported cases, by country, are available on the Internet website of the Office of International Des Epizooties, at http://www.oie.int/status/A_BSE.htm. These numbers should be interpreted with caution because of differences in the intensity of surveillance over time and by country. Information is being generated rapidly on BSE issues. Updated sources should be consulted.

Risk to Travelers

The current risk of acquiring nvCJD from eating beef (muscle meat) and beef products produced from cattle in Europe cannot be precisely determined, and this risk in specific countries might not reflect the fact that cattle products from one country might be distributed and consumed in others. Nevertheless, in the United Kingdom, this current risk appears to be extremely small, perhaps about 1 case per 10 billion servings. In the other countries of Europe, this current risk, if it exists at all, would not likely be any higher than that in the United Kingdom, except possibly in Portugal. In the 12-month period ending June 15, 2000, Portugal had about half the reported incidence of BSE cases per 1 million adult cattle as that reported in the United Kingdom; however, Portugal has less experience with implementing the BSE-related public health control measures.

Preventive Measures

Public health control measures, such as BSE surveillance, the culling of sick animals, or banning specified risk materials (SRMs), or a combination of these, have been instituted in Europe to prevent potentially BSE-infected tissues from entering the human food chain. The most stringent of these control measures have been applied in the United Kingdom and appear to have been highly effective. In June 2000, the European Union Commission on Food Safety and Animal Welfare adopted a decision requiring all member states to remove SRMs from animal feed and human food chains as of October 1, 2000; such bans had already been instituted in most member states.

To reduce the possible current risk of acquiring nvCJD from food, travelers to Europe should be advised to consider either (1) avoiding beef and beef products altogether or (2) selecting beef or beef products, such as solid pieces of muscle meat (versus brains or beef products such as burgers and

sausages), that might have a reduced opportunity for contamination with tissues that might harbor the BSE agent. Milk and milk products from cows are not believed to pose any risk for transmitting the BSE agent.

CHAGAS' DISEASE (AMERICAN TRYPANOSOMIASIS)

Description

Chagas' disease is caused by the protozoan parasite *Trypanosoma cruzi*. Acute infection can be asymptomatic or accompanied by a febrile illness with meningoencephalitis or myocarditis, or both. Manifestations of chronic infection include cardiomyopathy and intestinal "mega" syndromes (for example, megaesophagus and megacolon). Chagas' disease is usually transmitted by contact with the feces of an infected reduviid ("cone nose" or "kissing") bug; transmission can also occur through blood transfusion or via transplacental infection.

Occurrence

Chagas' disease occurs throughout much of the Western hemisphere, from Mexico to Argentina.

Risk for Travelers

Reduviid bugs typically infest buildings constructed of mud, adobe brick, or palm thatch, particularly those with cracks or crevices in the walls and roof. Avoiding overnight stays in dwellings infested by the reduviid bug vector greatly reduces the risk of acquiring the infection, and reports of acute Chagas' disease in travelers are rare. In some regions, travelers should be aware that blood for transfusion might not be routinely tested or treated for *T. cruzi*.

Preventive Measures

No vaccine is available. Preventive measures include insecticide spraying of infested houses and the use of bed netting. The latter should be recommended for travelers camping or sleeping out of doors in highly endemic areas.

Treatment

Anti-trypanosomal treatment exists for acute disease, and treatment can also be helpful for people with long-standing infection. Travelers should be advised to consult an infectious disease or tropical medicine specialist. People with chronic cardiac or mega-syndromes might benefit from symptomatic therapy.

CHOLERA

Description

Cholera is an acute intestinal infection caused by toxigenic *Vibrio cholerae* O-group 1 or O-group 139. The infection is often mild and self-limited or subclinical. People with severe cases respond dramatically to simple fluid- and electrolyte-replacement therapy. Infection is acquired primarily by ingesting contaminated water or food; person-to-person transmission is rare.

Occurrence

Since 1961, *V. cholerae* has spread from Indonesia through most of Asia into eastern Europe and Africa, and from North Africa to the Iberian Peninsula. In 1991, an extensive epidemic began in Peru and spread to neighboring countries in the Western Hemisphere. In 1999, nearly 255,000 cases from 61 countries were reported to the World Health Organization.

Risk for Travelers

People who follow usual tourist itineraries and who observe food safety recommendations while in countries reporting cholera have virtually no risk. Risk increases for those who drink untreated water or ingest poorly cooked or raw seafood in endemic areas.

Preventive Measures

Vaccine

The risk of cholera to U.S. travelers is so low that vaccination is of questionable benefit. At the present time, the manufacture and sale of the only licensed cholera vaccine in the United States (by Wyeth Ayerst) has been discontinued. It has not been recommended for travelers because of the brief and incomplete immunity it offers.

Two recently developed vaccines for cholera are licensed and available in other countries (Dukoral® from Biotec AB, and Mutacol® from Berna). Both vaccines appear to provide a somewhat better immunity and have fewer side effects than the previously available vaccine. However, neither of these two vaccines is recommended for travelers nor are they available in the United States. Further information on these vaccines can be obtained from the manufacturers at: Dukoral®, Active Biotec AB (publ), P.O. Box 724, SE-220 07, Lund, Sweden, telephone: 46 46 19 20 00, fax: 46 46 19 20 50, email: info@activebiotech.com, website: http://www.activebiotech.com; and Mutacol®, Berna, Switzerland Division, P.O. Box CH-3001, Berne, Switzerland, telephone: 41 31 981 22 11, fax: 41 31 981 20 66, email: berna@berna.org, website: http://www.berna.org/.

Currently, no country or territory requires vaccination as a condition for entry. Local authorities, however, may continue to require documentation of vaccination against cholera. In such cases, a single dose of either oral vaccine is sufficient to satisfy local requirements, or a medical waiver may be given.

Other

Travelers to cholera-affected areas should be advised to avoid eating high-risk foods, especially fish and shellfish. Food that is cooked and served hot, fruits and vegetables peeled by the traveler personally, and beverages and ice that are made from boiled or chlorinated water or that are carbonated are usually safe. (See Chapter 4, "Health Hints for the International Traveler," "Risks from Food and Drink," pages 165 through 168, for additional information.)

CRYPTOSPORIDIOSIS

Description

Cryptosporidiosis is a parasitic infection caused by *Cryptosporidium parvum* and occasionally other species of *Cryptosporidium*. It is transmitted by ingestion of fecally contaminated food or water, including water swallowed while swimming; by exposure to fecally contaminated environmental surfaces; and by the fecal-oral route from person to person (for example, while changing diapers, caring for an infected person, or engaging in certain sexual behaviors). Symptoms include watery diarrhea, abdominal cramps, vomiting, and fever. In immunocompetent people, symptoms last an average of 6 to 10 days. In people with severely weakened immune systems, cryptosporidiosis can become chronic and can be fatal.

Occurrence

Cryptosporidiosis occurs worldwide.

Risk for Travelers

For travelers to developing countries, risk of infection is highest for those with the greatest exposure to potentially contaminated food or water.

Preventive Measures

No vaccine is available. To avoid contracting cryptosporidiosis, travelers should be advised to follow the precautions described in Chapter 4, "Health Hints for the International Traveler," "Risks From Food and Drink," pages 165 through 168. Cryptosporidiosis is not inactivated by chlorine or iodine disinfection. Water can be treated effectively by boiling, or by filtration using an absolute 1-micron filter. Specific information on preventing cryptosporidiosis through filtration can be found in

"Preventing Cryptosporidiosis: A Guide to Water Filters and Bottled Water" at the following website: www.cdc.gov/ncidod/dpd/parasites/cryptosporidiosis/factsht_crypto_prevent_water.htm

Treatment

No antiparasitic drug has been found that can shorten the duration of infection. Travelers should be advised to consult with an infectious disease specialist.

CYCLOSPORIASIS

Description

Cyclospora cayetanensis, previously known as cyanobacterium-like, coccidia-like, and cyclospora-like bodies, is a protozoan parasite that causes gastrointestinal infection. Infection is acquired by ingestion of water or food contaminated with the parasite. Infection can be asymptomatic or be manifested by such symptoms as watery diarrhea, loss of appetite, weight loss, bloating, increased gas, stomach cramps, nausea, vomiting, fatigue, muscle aches, and low-grade fever. Some travelers first notice flu-like symptoms. If untreated, the illness can last for weeks to months.

Occurrence

Infection can be acquired worldwide.

Risk for Travelers

Travelers of all ages are at risk for infection. Travelers to developing countries can be at increased risk for this infection, and the risk can vary with the season. For example, travelers to Nepal are at increased risk for this infection from May through August.

Preventive Measures

No vaccine is available. Travelers to developing countries should be advised to follow the precautions in Chapter 4, "Health Hints for the International Traveler," "Risks From Food and Drink," pages 165 through 168. Direct, person-to-person transmission is unlikely.

Treatment

Specific treatment is available, and travelers should be advised to consult with an infectious disease specialist.

DENGUE FEVER

Description

Dengue fever and dengue hemorrhagic fever (DHF) are viral diseases transmitted by *Aedes* mosquitoes, usually *Aedes aegypti*. The four dengue viruses (DEN-1 through DEN-4) are immunologically related, but do not provide cross-protective immunity against each other. Dengue fever is characterized by sudden onset, high fever, severe frontal headache, and joint and muscle pain. Many patients have nausea, vomiting, and rash. The rash appears 3 to 5 days after onset of fever and can spread from the torso to the arms, legs, and face. The disease is usually benign and self-limited, although convalescence can be prolonged. Many cases of nonspecific viral syndrome or even subclinical infection occur, but dengue can also present as the severe, fatal hemorrhagic disease called DHF. There is no specific treatment for dengue infection.

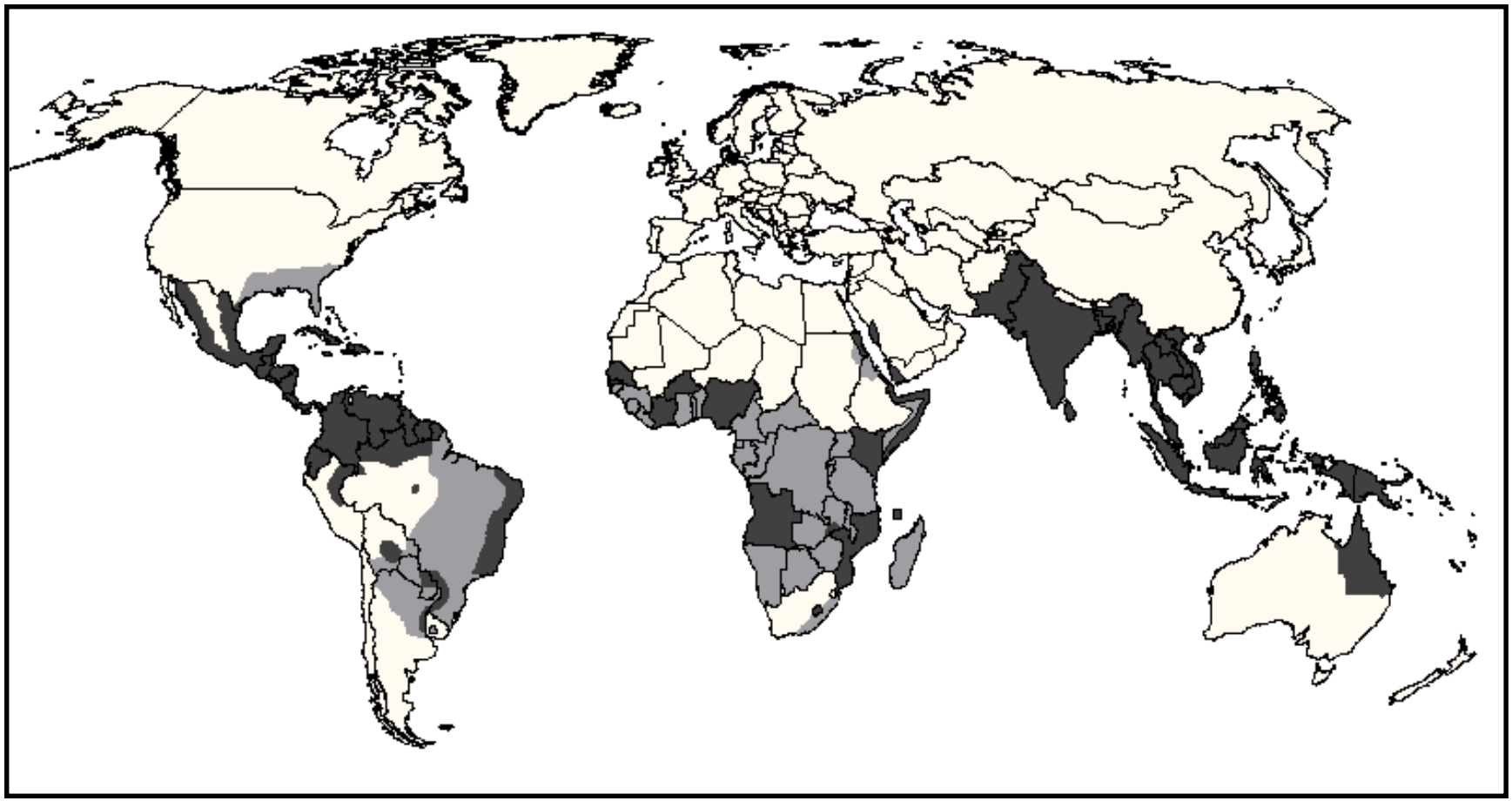
Occurrence

Dengue, a rapidly expanding disease in most tropical areas of the world, has become the most important arboviral disease of humans. There are now over 2.5 billion people living in areas at risk of infection and an estimated 50 to 100 million cases of dengue fever occur each year, 200,000 to 500,000 of which are DHF. The case-fatality rate for DHF averages 5%. Epidemics caused by all four virus serotypes have become progressively more frequent and larger in the past 20 years. As of 2000, dengue viruses had become endemic in most tropical countries of the South Pacific, Asia, the Caribbean basin, Mexico, Central and South America, and Africa (see Map 3-1). It is not possible to accurately predict future dengue incidence in specific locales, but increased dengue transmission is anticipated in all tropical areas of the world for the indefinite future. The incidence of the severe disease, DHF, has increased dramatically in Southeast Asia in the past 20 years, with major epidemics occurring in most countries every 3 to 5 years. DHF is an emerging disease in the Americas. The first major epidemic occurred in Cuba in 1981 and a second major epidemic of DHF occurred in Venezuela in 1989 and 1990. Since then, outbreaks or sporadic cases, or both, of confirmed DHF have occurred in 28 tropical American countries. After an absence of 35 years, a small number of autochthonous cases of dengue fever have been documented in the United States (southern Texas) in recent years associated with imported cases and epidemic dengue in adjacent states in Mexico.

Risk for Travelers

There is a risk of dengue infection for the international traveler, especially if an epidemic is in progress. Cases of dengue are confirmed every year in travelers returning to the United States following visits to tropical areas. Travelers to endemic and epidemic areas, therefore, should be advised to take precautions to avoid mosquito bites. The principal vector mosquito, *A. aegypti*, prefers to feed on humans during the daytime and most frequently is found in or near human habitations. There are two peak periods of biting activity, in the morning for several hours after

Map 3-1.—World Distribution of Dengue, 2000.



Areas infested with *Aedes aegypti*

Areas with *Aedes aegypti* and dengue epidemic activity

daybreak and in the late afternoon for several hours before dark. The mosquito can feed at any time during the day, however, especially indoors, in shady areas, or when it is overcast. Mosquito breeding sites include artificial water containers such as discarded tires, uncovered barrels, buckets, flower vases or pots, cans, and cisterns.

Although not completely understood, current data suggest that, in addition to virus strain, the immune status (that is, having had a previous dengue infection), age, and genetic background of the human host are the most important risk factors for developing DHF. In Asia, infants and children younger than 15 years of age who are experiencing a second dengue infection appear to have the highest risk, whereas in the Americas it is not uncommon for older children and adults to develop DHF. International travelers from nonendemic areas (such as the United States) are generally at low risk for DHF infection. There is little information in the medical literature about the risk of dengue infection in pregnant women. In spite of many epidemics, no increase in congenital malformations has been noted after dengue epidemics. A small number of recently reported cases suggests that if the mother is ill with dengue around the time of delivery, the child can be born with dengue or can acquire dengue through the delivery process itself.

Dengue should be considered by physicians in the differential diagnosis of all patients who present with fever and a history of travel to a tropical area within 3 weeks of onset of symptoms. Acetaminophen products are recommended for managing fever; acetylsalicyclic acid and nonsteroidal anti-inflammatory agents (that is, aspirin and ibuprofen) should be avoided because of their anticoagulant properties. For diagnosis, acute- and convalescent-phase serum samples should be obtained and sent through state or territorial health department laboratories to the Centers for Disease Control and Prevention's Dengue Branch, Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases, 1324 Calle Cañada, San Juan, Puerto Rico 00920-3860. Serum samples should be accompanied by clinical and epidemiologic information, including the date of disease onset, the date of collection of the sample, and a detailed recent travel history. For additional information, the Dengue Branch can be contacted at: telephone 1-787-706-2399; fax 1-787-706-2496; or email, hseda@cdc.gov.

Preventive Measures

No vaccine is available. Travelers should be advised that they can reduce their risk of acquiring dengue by remaining in well-screened or air-conditioned areas when possible, by wearing clothing that adequately covers the arms and legs, and by applying insect repellent to both skin and clothing. The most effective repellents are those containing N,N-diethylmetatoluamide (DEET) at a concentration of #35%. High concentration (>35% DEET) products for the skin, particularly for children, should be avoided. (See Chapter 4, "Health Hints for the International Traveler," "Protection Against Mosquitoes and Other Arthropod Vectors," pages 163 through 165.)

DIPHTHERIA, TETANUS, AND PERTUSSIS

Description

Diphtheria is an acute bacterial disease involving primarily the tonsils, pharynx, larynx, nose, and occasionally other mucous membranes of skin. The characteristic lesion is marked by a patch or patches of an adherent grayish membrane with a surrounding inflammation.

Tetanus is an acute disease induced by an exotoxin of the tetanus bacillus, which grows anaerobically at the site of an injury. The disease is characterized by painful muscular contractions, primarily of the masseter and other large muscles.

Pertussis is an acute bacterial disease involving the respiratory tract, characterized by paroxysmal coughing.

Occurrence

Diphtheria remains a serious disease throughout much of the world. In particular, large outbreaks of diphtheria occurred in the 1990s throughout Russia and the independent countries of the former Soviet Union. Most cases occurred in unimmunized or inadequately immunized people. Control measures have been implemented, but a risk of diphtheria remains in all these areas.

Tetanus is a global health problem. The disease occurs almost exclusively in people who are unimmunized or inadequately immunized. In developing countries, most reported illness occurs in infants and young children.

Pertussis occurs primarily in children and is common in countries where immunization is not generally provided. Pertussis can also occur in adults after immunity from vaccines has waned. It is highly communicable, is often associated with complications, and has a relatively high case-fatality ratio in infants.

Risk for Travelers

Diphtheria and pertussis are more common in parts of the world where immunization levels are low. Tetanus can occur in an unvaccinated person anywhere in the world.

Preventive Measures

Vaccine

Immunizations for Infants and Children Younger Than 7 Years of Age

Simultaneous immunization against diphtheria, tetanus, and pertussis during infancy (see Tables 1-2 and 1-3) is recommended. Neither whole-cell (DTP) nor acellular (DTaP) pertussis vaccine is licensed for people 7 years of age or older. Pertussis vaccination is not recommended after a child's seventh birthday.

Combination vaccines containing either DTP or DTaP pertussis vaccine are available in the United States. DTaP is the preferred vaccine for all doses of the diphtheria, tetanus, and pertussis vaccination series. DTP may be used if DTaP is not readily available. Since February 1999, four brands of DTaP have been licensed in the United States, all of which contain different numbers and concentrations of pertussis antigen. There is no documented evidence that one brand of DTaP is more efficacious or safer than the other brands. Neither the Advisory Committee on Immunization Practices (ACIP) nor the American Academy of Pediatrics prefers one brand over another.

Primary immunization for infants and children up to their seventh birthday consists of four doses of DTaP vaccine (Table 1-2). The first dose is typically given when an infant is 2 months of age. The first three doses should be given at 4- to 8-week intervals, with the fourth dose given when the infant is 15 to 18 months of age. A fifth (booster) dose is recommended when the child is 4 to 6 years of age. The fifth dose is not necessary if the fourth dose in the primary series was given after the child's fourth birthday.

At least three, and preferably four, doses of DTaP are necessary for protection against pertussis. Travelers should be advised to complete as many doses as possible of the primary series before traveling to an area with increased risk of pertussis. If an accelerated schedule is required to complete the series, the schedule may be started as soon as the infant is 6 weeks of age, with the second and third doses given 4 weeks after each preceding dose (see Table 1-3). The fourth dose should not be given before the child is 12 months of age and should be separated from the third dose by at least 6 months. The fifth (booster) dose should not be given before the child is 4 years of age.

Interruption of the recommended schedule or delay in doses does not lead to a reduction in the level of immunity reached on completion of the primary series. There is no need to restart a series regardless of the time that has elapsed between doses.

DTaP vaccines are as efficacious as DTP vaccines when administered to infants and children as the primary series. In addition, local reactions, fever, and other systemic adverse events occur substantially less often after DTaP administration than after administration of DTP. As a result, DTaP vaccines are recommended for all five doses of the vaccination schedule. For infants and children who

have started the vaccination series with DTP, DTaP may be substituted for any doses of the pertussis series. A pertussis vaccination series begun with DTP may be completed with DTaP.

There are no data regarding the safety, immunogenicity, and efficacy of using DTaP vaccines from different manufacturers for successive doses of the primary or booster vaccination series ("mix and match"). Whenever possible, the same brand of DTaP vaccine should be used for all doses of the vaccination series. However, the type of vaccine previously administered might not be known, or the type of vaccine used for earlier doses might not be available. In such circumstances, any licensed DTaP vaccine may be used to continue or complete the vaccination series. Vaccination should NOT be deferred because the type of DTaP used for earlier doses is not available.

Reducing the dose of DTP or DTaP vaccine or giving the full dose in multiple smaller doses can result in an altered immune response and inadequate protection. Furthermore, there is no evidence that the frequency of significant vaccine reactions is likely to be reduced by this practice. The use of multiple, reduced doses that together equal a full immunizing dose or the use of smaller, divided doses is not endorsed or recommended. Any vaccination using less than the standard dose or a nonstandard route or site of administration should not be counted, and the infant or child should be revaccinated according to his or her age.

Infants and children inadequately immunized for their age should be brought up to date prior to travel. For infants and children younger than 7 years of age with a contraindication to the pertussis component of DTaP, diphtheria-tetanus (DT) should be used (Table 1-3).

Immunizations for Children 7 Years of Age or Older, Adolescents, and Adults

Unvaccinated children 7 years of age or older, adolescents, and adults should receive three doses of the adult formulation of tetanus-diphtheria toxoid (Td) (Table 1-4). The use of Td is recommended whenever either tetanus or diphtheria toxoid is indicated. The first two doses should be given 4 to 8 weeks apart and the third dose 6 to 12 months after the second. Two doses of Td received at intervals of at least 4 weeks can provide some protection, while a single dose is of little benefit. Anyone who cannot provide written documentation of having received a complete series of tetanus and diphtheria toxoids should be given a three-dose series.

The first booster dose of Td should be given when the child is 11 or 12 years of age if at least 5 years has elapsed since the last dose of DTaP, DTP, or pediatric DT. A booster dose of Td should be given every 10 years thereafter.

Adverse Reactions

Local reactions (generally erythema and induration with or without tenderness) are common after the administration of vaccines containing diphtheria, tetanus, and pertussis antigens. Mild systemic reactions such as fever, drowsiness, fretfulness, and low-grade fever can occur after vaccination with either DTP or DTaP. However, even mild reactions following the first four doses are less common

among children who receive DTaP. For instance, fever >38.3° Celsius (C) (>101° Fahrenheit [F]) is reported in 3% to 5% of DTaP recipients, compared with 16% of DTP recipients. These reactions are self-limited and can be managed with symptomatic treatment of acetaminophen or ibuprofen. Moderate to severe systemic events (for example, fever $40.5° C [$105° F], febrile seizures, persistent crying lasting 3 hours or more, and hypotonic-hyporesponsive episodes) have been reported rarely after administration of DTaP, and they have occurred less frequently among children administered DTaP than among children administered DTP.

Rarely, anaphylactic reactions have been reported after receipt of a preparation containing diphtheria, tetanus or pertussis, or a combination of these. Arthus-type hypersensitivity reactions, characterized by severe local reactions, can follow receipt of tetanus and diphtheria toxoids, particularly in adults who have received frequent (for example, annual) boosters of tetanus or diphtheria toxoids, or a combination of the two. The rates of local reactions, fever, and other common systemic symptoms following receipt of DTaP are lower than those following DTP vaccination.

Precautions and Contraindications

A severe allergic reaction to a prior dose of vaccine or vaccine component is a contraindication to further vaccination with DTaP, DTP, DT, or adult Td. Encephalopathy not due to another identifiable cause within 7 days of vaccination is a contraindication to further vaccination with a pertussis-containing vaccine.

Moderate or severe acute illness can be a contraindication to vaccination. Anyone with mild illnesses, such as otitis media or upper respiratory infection, should be vaccinated. Anyone for whom vaccination is deferred because of moderate or severe acute illness should be vaccinated when his or her condition improves.

Certain infrequent adverse events following pertussis vaccination will generally contraindicate subsequent doses of pertussis vaccine. These adverse events include temperature a $40.5° C ($105° F) not resulting from another identifiable cause; collapse or a shock-like state (hypotonic-hyporesponsive episode) or persistent, inconsolable crying lasting 3 hours or more and occurring within 48 hours of vaccination (applicable to infants and children); and convulsions with or without fever occurring within 3 days of vaccination. There might be circumstances (for example, during a communitywide outbreak of pertussis) in which the benefit of vaccination outweighs the risk, even if one of the four precautionary adverse events occurred following a previous dose. Under these circumstances, one or more additional doses of pertussis vaccine may be considered. DTaP should be used in these circumstances.

DTaP vaccine should NOT be substituted in infants and children who have a valid contraindication to DTP vaccine. If a valid contraindication or precaution exists, DT should be used for the remaining doses in the schedule.

Neurologic conditions characterized by changing developmental findings are considered contraindications to receipt of pertussis vaccine. Such disorders include uncontrolled epilepsy,

infantile spasms, and progressive encephalopathy. An infant who, because of perinatal complications or other conditions, is felt to be at an increased risk of latent onset of central nervous system disorders should have immunization with DTaP or DT delayed until further observation and study have clarified the infant's neurologic status. The decision whether to commence immunization with DTaP or with DT should be made no later than an infant's first birthday. Infants and children with stable neurologic conditions such as cerebral palsy or well-controlled seizures **should** be vaccinated. The occurrence of a single seizure (not temporally associated with DTaP) does not contraindicate DTaP vaccination, particularly if the seizures can be satisfactorily explained. Parents of infants and children with personal or family histories of convulsion should be informed of the increased risk of simple febrile seizures following immunization. Acetaminophen (15 milligrams per kilogram, every 4 hours for 24 hours) should be given to infants and children with such histories to reduce the possibility of postvaccination fever. Infants and children who have received more than one dose of DTaP and who experience a neurologic disorder (for example, a seizure) not temporally associated with the vaccination, but before the next scheduled dose, should have their neurologic status evaluated and clarified before a subsequent dose of DTaP is given.

ENCEPHALITIS, JAPANESE

Description

Japanese encephalitis (JE) is a common mosquito-borne viral encephalitis found in Asia. Most infections are asymptomatic, but among people who develop a clinical illness, the case-fatality rate can be as high as 30%. Neuropsychiatric sequelae are reported in 50% of survivors. In endemic areas, children are at greatest risk of infection; however, multiple factors such as occupation, recreational exposure, sex (possibly reflecting exposure), previous vaccination, and naturally acquired immunity alter the potential for infection and illness. A higher case-fatality rate is reported in the elderly, but serious sequelae are more frequent in the very young, possibly because they are more likely to survive a severe infection.

JE virus is transmitted chiefly by the bites of mosquitoes in the *Culex vishnui* complex; the individual vector species in specific geographic areas differ. In China and many endemic areas in Asia, *Culex tritaeniorhyncus* is the principal vector. This species feeds outdoors beginning at dusk and during evening hours until dawn; it has a wide host range, including domestic animals, birds, and humans. Larvae are found in flooded rice fields, marshes, and small stable collections of water around cultivated fields. In temperate zones, the vectors are present in greatest numbers from June through September and are inactive during winter months. Swine and certain species of wild birds function as viremic amplifying hosts in the transmission cycle.

Occurrence

Habitats supporting the transmission cycle of JE virus are principally in rural, agricultural locations. In many areas of Asia, however, the appropriate ecologic conditions for virus transmission occur near or occasionally within urban centers. Transmission is seasonal and occurs in the summer and autumn

in the temperate regions of China, Japan, Korea, and eastern areas of Russia. Elsewhere, seasonal patterns of disease are more extended or vary with the rainy season and irrigation practices. Risk of JE varies by season and geographic area (Table 3-1).

Risk for Travelers

The risk to short-term travelers and those who confine their travel to urban centers is very low. Expatriates and travelers living for prolonged periods in rural areas where JE is endemic or epidemic are at greatest risk. Travelers with extensive unprotected outdoor, evening, and nighttime exposure in rural areas, such as might be experienced while bicycling, camping, or engaging in certain occupational activities, might be at high risk even if their trip is brief.

Preventive Measures

Vaccine

JE vaccine licensed in the United States is manufactured by Biken, Osaka, Japan, and distributed by Aventis Pasteur. Other JE vaccines are made by several companies in Asia, but are not licensed in the United States. Vaccination should be considered only by people who plan to live in areas where JE is endemic or epidemic and by travelers whose activities include trips into rural, farming areas. Short-term travelers (less than 30 days), especially those whose visits are restricted to major urban areas, are at lower risk for acquiring JE and generally should not be advised to receive the vaccine. Evaluation of an individual traveler's risk should take into account his or her itinerary and activities and the current level of JE activity in the country (see Table 3-1).

The recommended primary immunization series is three doses of 1.0 milliliter (mL) each, administered subcutaneously on days 0, 7, and 30. An abbreviated schedule of days 0, 7, and 14 can be used when the longer schedule is impractical because of time constraints. Two doses given a week apart may be used in unusual circumstances, but will confer short-term immunity in only 80% of vaccinees. The last dose should be administered at least 10 days before commencement of travel to ensure an adequate immune response and access to medical care in the event of delayed adverse reactions (Table 3-2).

Immunization routes and schedules for infants and children 1 through 3 years of age are identical except that doses of 0.5 mL should be administered. No data are available on vaccine efficacy and safety in infants younger than 1 year of age. The full duration of protection is unknown; however, preliminary data indicate that neutralizing antibodies persist for at least 2 years after primary immunization. In infants and children whose primary immunization series included doses of 0.5 mL, a booster dose of 1.0 mL (0.5 mL for children younger than 3 years of age) may be administered 2 years after the primary series.

Table 3-1.—Risk of Japanese Encephalitis, by Country, Region, and Season.

COUNTRY	AFFECTED AREAS	TRANSMISSION SEASON	COMMENTS
Australia	Islands of Torres Strait.	Probably year-round transmission risk.	Localized outbreak in Torres Strait in 1995 and sporadic cases in 1998 in Torres Strait and on mainland Australia at Cape York Peninsula.
Bangladesh	Few data, but probably widespread.	Possibly July to December, as in northern India.	Outbreak reported from Tangail District, Dacca Division; sporadic cases in Rajshahi Division.
Bhutan	No data.	No data.	No comments.
Brunei	Presumed to be sporadic-endemic as in Malaysia.	Presumed year-round transmission.	No comments.
Burma	Presumed to be endemic-hyperendemic countrywide.	Presumed to be May to October.	Repeated outbreaks in Shan State in Chiang Mai valley.
Cambodia	Presumed to be endemic-hyperendemic countrywide.	Presumed to be May to October.	Cases reported from refugee camps on Thai border.
India	Reported cases from all states except Arunachal, Dadra, Daman, Diu, Gujarat, Himachal, Jammu, Kashmir, Lakshadweep, Meghalaya, Nagar Haveli, Orissa, Punjab, Rajasthan, and Sikkim.	South India: May to October in Goa; October to January in Tamil Nadu; and August to December in Karnataka. Second peak, April to June in Mandya District. Andrha Pradesh: September to December. North India: July to December.	Outbreaks in West Bengal, Bihar, Karnataka, Tamil Nadu, Andrha Pradesh, Assam, Uttar Pradesh, Manipur, and Goa. Urban cases reported (for example, Luchnow).

Indonesia	Kalimantan, Bali, Nusa, Tenggara, Sulawesi, Mollucas, and Irian Jaya (Papua), and Lombok.	Probably year-round risk; varies by island; peak risks associated with rainfall, rice cultivation, and presence of pigs. Peak periods of risk: November to March; June and July in some years.	Human cases recognized on Bali, Java, and possibly in Lombok.
Japan*	Rare-sporadic cases on all islands except Hokkaido.	June to September, except April to December on Ryuku Islands (Okinawa).	Vaccine not routinely recommended for travel to Tokyo and other major cities. Enzootic transmission without human cases observed on Hokkaido.
Korea	North Korea: No data. South Korea: Sporadic-endemic with occasional outbreaks.	July to October.	Last major outbreaks in 1982 and 1983. Sporadic cases reported in 1994 and 1998.
Laos	Presumed to be endemic–hyperendemic country-wide.	Presumed to be May to October.	No comments
Malaysia	Sporadic–endemic in all states of Peninsula, Sarawak, and probably Sabah.	Year-round transmission.	Most cases from Penang, Perak, Salangor, Johore, and Sarawak.
Nepal	Hyperendemic in southern lowlands (Terai).	July to December.	Vaccine not recommended for travelers visiting only high-altitude areas.
Pakistan	May be transmitted in central deltas.	Presumed to be June to January.	Cases reported near Karachi; endemic areas overlap those for West Nile virus. Lower Indus Valley might be an endemic area.
Papua New Guinea	Normanby Islands and Western Province.	Probably year-round risk.	Localized sporadic cases.

Table 3-1.—Continued.

COUNTRY	AFFECTED AREAS	TRANSMISSION SEASON	COMMENTS
People's Republic of China	Cases in all provinces except Xizang (Tibet), Xinjiang, Qinghai. Hyperendemic in southern China. Endemic–periodically epidemic in temperate areas. Hong Kong: Rare cases in new territories. Taiwan: Endemic, sporadic cases; islandwide.*	Northern China: May to September. Southern China: April to October (Guangxi, Yunnan, Guangdong, and Southern Fujian, Sichuan, Guizhou, Hunan, and Jiangxi provinces). Hong Kong: April to October. Taiwan: April to October, with a June peak.*	Vaccine not routinely recommended for travelers to urban areas only. Taiwan: Cases reported in and around Taipei and the Kao-hsiung–Pingtung river basins.*
Philippines	Presumed to be endemic on all islands.	Uncertain; speculations based on locations and agroecosystems. West Luzon, Mindoro, Negros, Palawan: April to November. Elsewhere: year-round, with greatest risk April to January.	Outbreaks described in Nueva Ecija, Luzon, and Manila.
Russia	Far Eastern maritime areas south of Khabarousk.	Peak period July to September.	First human cases in 30 years recently reported.
Singapore	Rare cases.	Year-round transmission, with April peak.	Vaccine not routinely recommended.
Sri Lanka	Endemic in all but mountainous areas. Periodically epidemic in northern and central provinces.	October to January; secondary peak of enzootic transmission May to June.	Recent outbreaks in central (Anuradhapura) and northwestern provinces.
Thailand	Hyperendemic in north; sporadic endemic in south.	May to October.	Annual outbreaks in Chiang Mai Valley; sporadic cases in Bangkok suburbs.

Vietnam	Endemic–hyperendemic in all provinces.	May to October.	Highest rates in and near Hanoi.
Western Pacific	Two epidemics reported in Guam and Saipan since 1947.	Uncertain; possibly September to January.	Enzootic cycle might not be sustainable; epidemics might follow introductions of virus.

*Local JE incidence rates might not accurately reflect risks to nonimmune visitors because of high immunization rates in local populations. Humans are incidental to the transmission cycle. High levels of viral transmission can occur in the absence of human disease.

NOTE: Assessments are based on publications, surveillance reports, and personal correspondence. Extrapolations have been made from available data. Transmission patterns can change.

Table 3-2.—Japanese Encephalitis Vaccine.

DOSES	SUBCUTANEOUS ROUTE		COMMENTS
	1 through 2 Years of Age	3 Years of Age or Older	
Primary series 1, 2, and 3	0.5 milliliter	1.0 milliliter	Days 0, 7, and 30
Booster*	0.5 milliliter	1.0 milliliter	1 dose at 24 months or later

*In vaccinees who have completed a three-dose primary series, the full duration of protection is unknown; therefore, definitive recommendations cannot be given.

Adverse Reactions

JE vaccine is associated with local reactions and mild systemic side effects (fever, headache, myalgias, and malaise) in about 20% of vaccinees. More serious allergic reactions, including generalized urticaria, angioedema, respiratory distress, and anaphylaxis, have occurred within minutes to as long as one week after immunization. Such hypersensitivity reactions occur in approximately 0.6% of vaccinees. Reactions have been responsive to therapy with epinephrine, antihistamines, or steroids, or a combination of these. Vaccinees should be observed for 30 minutes after immunization and warned about the possibility of delayed allergic reactions. The full course of immunization should be completed at least 10 days before departure, and vaccinees should be advised to remain in areas with access to medical care. People with a past history of urticaria appear to have a greater risk for developing more serious allergic reactions, and this must be considered when weighing the risks and benefits of the vaccine. A history of allergy to JE or other mouse-derived vaccines is a contraindication to further immunization.

Precautions and Contraindications

People with known hypersensitivity to the vaccine should not be vaccinated. People with multiple allergies, especially a history of allergic urticaria or angioedema, are at higher risk for allergic complications for JE vaccine.

Pregnancy.—Vaccination during pregnancy should be avoided unless the risk of acquiring JE outweighs the theoretical risk of vaccination.

Other

Travelers should be advised to stay in screened or air-conditioned rooms, to use bed nets when such quarters are unavailable, to use aerosol insecticides and mosquito coils as necessary, and to use insect repellents and protective clothing to avoid mosquito bites.

ENCEPHALITIS, TICKBORNE

Description

Tickborne encephalitis (TBE), also known as spring-summer encephalitis, is a viral infection of the central nervous system transmitted by bites of certain vector ticks. Human infections follow bites of infected *Ixodes ricinus* ticks, usually in people who visit or work in forests, fields, or pastures. Infection also can be acquired by consuming unpasteurized dairy products from infected cows, goats, or sheep.

Occurrence

The disease occurs in Scandinavia, western and central Europe, and countries that made up the former Soviet Union. Risk of acquiring the disease is greatest from April through August, when *Ixodes ricinus*, the principal tick vector, is most active. TBE is common in Austria, Estonia, Latvia, the Czech Republic, Slovakia, Germany, Hungary, Poland, Switzerland, Russia, Ukraine, Belarus, and northern Yugoslavia. It occurs at a lower frequency in Bulgaria; Romania; Denmark; France; the Aland archipelago and neighboring Finnish coastline; and along the coastline of southern Sweden, from Uppsala to Karlshamn. Serologic evidence for TBE infection, as well as sporadic cases, has been reported from Albania, Greece, Italy, Norway, and Turkey. A closely related disease, Russian spring-summer encephalitis, transmitted by *Ixpersulcatus* ticks, occurs in China, Korea, Japan, and eastern areas of Russia. The severity of disease, incidence of sequelae, and case-fatality rates are higher in the Far East and eastern regions of Russia than in western and central Europe.

Risk to Travelers

The risk to travelers who do not visit forested areas or consume unpasteurized dairy products is low. Travelers with extensive unprotected outdoor, evening, and nighttime exposure in rural areas, such as might be experienced while bicycling, camping, or engaging in certain occupational activities, might be at high risk even if their trip is brief.

Preventive Measures

Vaccine

Although effective vaccines can be obtained in Europe from Baxter (Vienna, Austria, and Behring, Germany) available data do not support recommending its use by those traveling less than 3 weeks. Anyone traveling longer than 3 weeks should be advised to obtain the vaccine if he or she plans to be in infected areas during the warm weather months when ticks are active.

Other

Travelers should be advised to avoid tick-infested areas and to protect themselves from tick bites by dressing appropriately and using repellents. Repellents containing N,N-diethylmetatoluamide (DEET) can be applied directly on the skin. Compounds containing permethrin have an acaricidal and repellent effect and should be used on clothing and camping gear. (See Chapter 4, "Health Hints for the International Traveler," "Protection Against Mosquitoes and Other Arthropod Vectors," pages 163 through 165.) Consumption of unpasteurized dairy products should be avoided.

FILARIASIS, LYMPHATIC

Description

Lymphatic filariasis is caused primarily by adult worms (filariae) that live in the lymphatic vessels. The female worms release microfilariae that circulate in the peripheral blood and are ingested by mosquitoes; thus, infected mosquitoes transmit the infection from person to person. The two major species of filariae that cause lymphatic disease in humans are *Wuchereria bancrofti* and *Brugia malayi*. Clinical manifestations include asymptomatic infection, acute inflammation of the lymph nodes and lymphatic vessels, tropical pulmonary eosinophilia, lymphedema that can progress to elephantiasis, and testicular hydrocele.

Occurrence

Lymphatic filariasis affects an estimated 120 million people in tropical areas of the world, including sub-Saharan Africa, Egypt, southern Asia, the western Pacific islands, the northeastern coasts of South and Central America, and the Caribbean islands.

Risk to Travelers

Short-term travelers to endemic areas are at low risk for this infection. Travelers who visit endemic areas for extended periods of time and who are intensively exposed to infected mosquitoes can become infected. Most infections seen in the United States are in immigrants from endemic countries.

Preventive Measures

No vaccine is available, nor has the effectiveness of chemoprophylaxis been well documented. Protective measures include avoidance of mosquito bites through the use of personal protection measures such as those outlined in Chapter 4, "Health Hints for the International Traveler," "Protection Against Mosquitoes and Other Arthropod Vectors," pages 163 through 165.

Treatment

The drug of choice for treatment of travelers with *W. bancrofti* or *B. malayi* infections is diethylcarbamazine (DEC). DEC, available to U.S.-licensed physicians for this purpose, can be obtained from the Parasitic Diseases Drug Service at the Centers for Disease Control and Prevention (CDC) at 404-639-3670. DEC kills circulating microfilaria and is partially effective against the adult worms. For chronic manifestations of lymphatic filariasis, such as lymphedema and hydrocele, specific lymphedema treatment and surgical repair, respectively, are recommended. Travelers should be advised to consult an infectious disease or tropical medicine specialist.

GIARDIASIS

Description

Giardiasis is a diarrheal illness caused by a microscopic parasite (*Giardia intestinalis*) that lives in the intestines of people and animals. Symptoms occur approximately 1 to 2 weeks after ingestion of the parasite and include diarrhea, abdominal cramps, bloating, fatigue, weight loss, flatulence, anorexia, or nausea, in various combinations, and usually last more than 5 days. Fever and vomiting are uncommon. The parasite is passed in the feces of an infected person or animal. Transmission occurs from ingestion of fecally contaminated food or drinking or recreational water, from exposure to fecally contaminated environmental surfaces, and from person to person by the fecal-oral route.

Occurrence

Giardiasis occurs worldwide.

Risk for Travelers

Risk of infection increases with duration of travel and is highest for those who live in or visit rural areas, trek in back country areas, or frequently eat or drink in areas that have poor sanitation and inadequate drinking water treatment facilities.

Preventive Measures

No vaccine is available and there is no known chemoprophylaxis. To prevent infection, travelers to disease-endemic areas should be advised to follow the precautions included in Chapter 4, “Health Hints for the Traveler,” pages 161 through 190.

Treatment

Effective antimicrobial drugs are available. Travelers should be advised that treatment recommendations are available in a variety of textbooks on internal medicine and infectious diseases, or that consultation with a travel medicine specialist is recommended.

HAEMOPHILUS INFLUENZAE TYPE B MENINGITIS AND INVASIVE DISEASE

Description

Haemophilus influenzae type b (Hib) causes meningitis and other severe bacterial infections (for example, pneumonia, septic arthritis, epiglottitis, and sepsis), primarily among infants and children younger than 5 years of age. Because the Hib vaccine is used widely in the United States, the highest rate of reported invasive Hib disease is among infants younger than 6 months of age; the incidence among infants and children 1 through 4 years of age is much lower than among infants younger than 1 year of age. The disease is rarely reported in anyone 5 years of age or older. Most cases occur in infants and children who are unvaccinated or incompletely vaccinated.

Occurrence

In the early 1980s (before licensure of conjugate Hib vaccines), it was estimated that about 20,000 cases of invasive Hib disease occurred annually in the United States, primarily among infants and children younger than 5 years of age. As a result of the widespread use of conjugate Hib vaccines, the disease is now uncommon in the United States, with fewer than 200 cases reported annually.

Risk for Travelers

Invasive Hib disease occurs throughout the world. Few countries routinely use Hib vaccine, so invasive Hib disease remains common in many countries.

Preventive Measures

Vaccine

Three different conjugate Hib vaccines are licensed for use in infants: HbOC (HibTiTER®, Wyeth-Lederle), PRP-OMP (PedvaxHIB®, Merck & Co., Inc.), and PRP-T (ActHIB®, Aventis Pasteur, and OmniHIB®, GlaxoSmithKline). A fourth Hib conjugate vaccine, PRP-D (ProHIBIT®, Aventis Pasteur), is licensed only for infants and children 12 through 60 months of age and should not be used for the primary series. PRP-OMP vaccine is available combined with hepatitis B vaccine (Comvax®). HbOC and PRP-T are also available combined with whole-cell pertussis vaccine

Table 3-3.—Recommended *Haemophilus influenzae* Type b (Hib) Routine Vaccination Schedule.

VACCINE	2 MONTHS	4 MONTHS	6 MONTHS	12 TO 15 MONTHS
HbOC/PRP–T	Dose 1	Dose 2	Dose 3	Booster
PRP–OMP	Dose 1	Dose 2	----------	Booster
PRP-D*	----------	----------	----------	Single dose

*PRP-D is licensed for a booster dose following a primary series of another type of vaccine when the infant is 12 months of age and for a single dose in previously unvaccinated infants at 15 months of age.

(Tetramune and ActHIB®/DTP, respectively). PRP-T (ActHIB®) is also available combined with acellular pertussis vaccine (DTaP Tripedia®) (the combined product is called TriHIBit). However, since February 1999, TriHIBit has been licensed for use only as the fourth dose of the Hib and DTaP series. It should not be given for the first, second, or third doses of the Hib series.

All infants, including those born prematurely, should receive a primary series of conjugate Hib vaccine (separate or as a combination vaccine), beginning at 2 months of age. The number of doses in the primary series depends on the type of vaccine used. A primary series of PRP-OMP (PedvaxHIB®) vaccine is two doses; HbOC (HibTiTER®) and PRP-T (ActHIB® and OmniHIB®) require a three-dose primary series (see Table 3-3). A booster should be given at 12 to 15 months of age, regardless of which vaccine is used for the primary series.

The optimal interval between doses is 2 months, with a minimum interval of 1 month. At least 2 months should separate the booster dose from the previous (second or third) dose. Hib vaccines may be given simultaneously with all other vaccines.

Data suggest that if Hib conjugate vaccines are given to infants younger than 6 weeks of age, they can induce immunologic tolerance to additional doses of Hib vaccine. Therefore, Hib vaccines, including combination vaccines that contain Hib conjugate, should never be given to a child younger than 6 weeks of age.

All three conjugate Hib vaccines licensed for use in infants are interchangeable. A series that includes vaccines of more than one type will induce a protective antibody level. If it is necessary to change the type of vaccine, three doses of any combination constitute the primary series. Any licensed conjugate vaccine may be used for the booster dose, regardless of what was received in the primary series.

Unvaccinated infants and children 7 months of age or older might not require a full series of three or four doses. The number of doses an infant or a child needs to complete the series depends primarily on the infant's or child's age at the time and, to a lesser degree, on the number of prior doses of Hib vaccine received. Previously unvaccinated infants and children 15 through 60 months of age should receive a single dose of any conjugate Hib vaccine. In general, children older than 60 months of age do not need Hib vaccination. Refer to the American Academy of Pediatrics Red Book for additional information on late or lapsed Hib vaccination schedules.

Adverse Reactions

Adverse events following vaccination with Hib conjugates are uncommon. Swelling, redness, or pain, or a combination of these, have been reported in 5% to 30% of recipients and usually resolve within 12 to 24 hours. Systemic reactions such as fever and irritability are infrequent. Information on adverse events suggests that the risks for local and systemic events following Tetramune and ActHIB®/DTP administration are similar to those following concurrent administration of their individual component vaccines and are probably due to the pertussis component of the DTP vaccine.

Precautions and Contraindications

Vaccination with Hib conjugate vaccine is contraindicated in anyone known to have experienced anaphylaxis following a prior dose of that vaccine. Vaccination should be delayed in infants and children with moderate or severe acute illnesses. Minor illnesses (for example, mild upper respiratory infection) are not contraindications to vaccination. Contraindications and precautions for the use of Tetramune, ActHIB®/DTP, TriHIBit, and Comvax® are the same as those for their individual component vaccines (that is, DTP, DTaP, Hib, and hepatitis B).

HEPATITIS, VIRAL, TYPE A

Description

Hepatitis A is an enterically transmitted viral disease that causes fever, malaise, anorexia, nausea, and abdominal discomfort, followed within a few days by jaundice. The disease ranges in clinical severity from no symptoms to a mild illness lasting 1 to 2 weeks to a severely disabling disease lasting several months. In developing countries, hepatitis A virus (HAV) is usually acquired during childhood, most frequently as an asymptomatic or mild infection. Transmission can occur by direct person-to-person contact; through exposure to contaminated water, ice, or shellfish harvested from sewage-contaminated water; or from fruits, vegetables, or other foods that are eaten uncooked, and which can become contaminated during harvesting or subsequent handling.

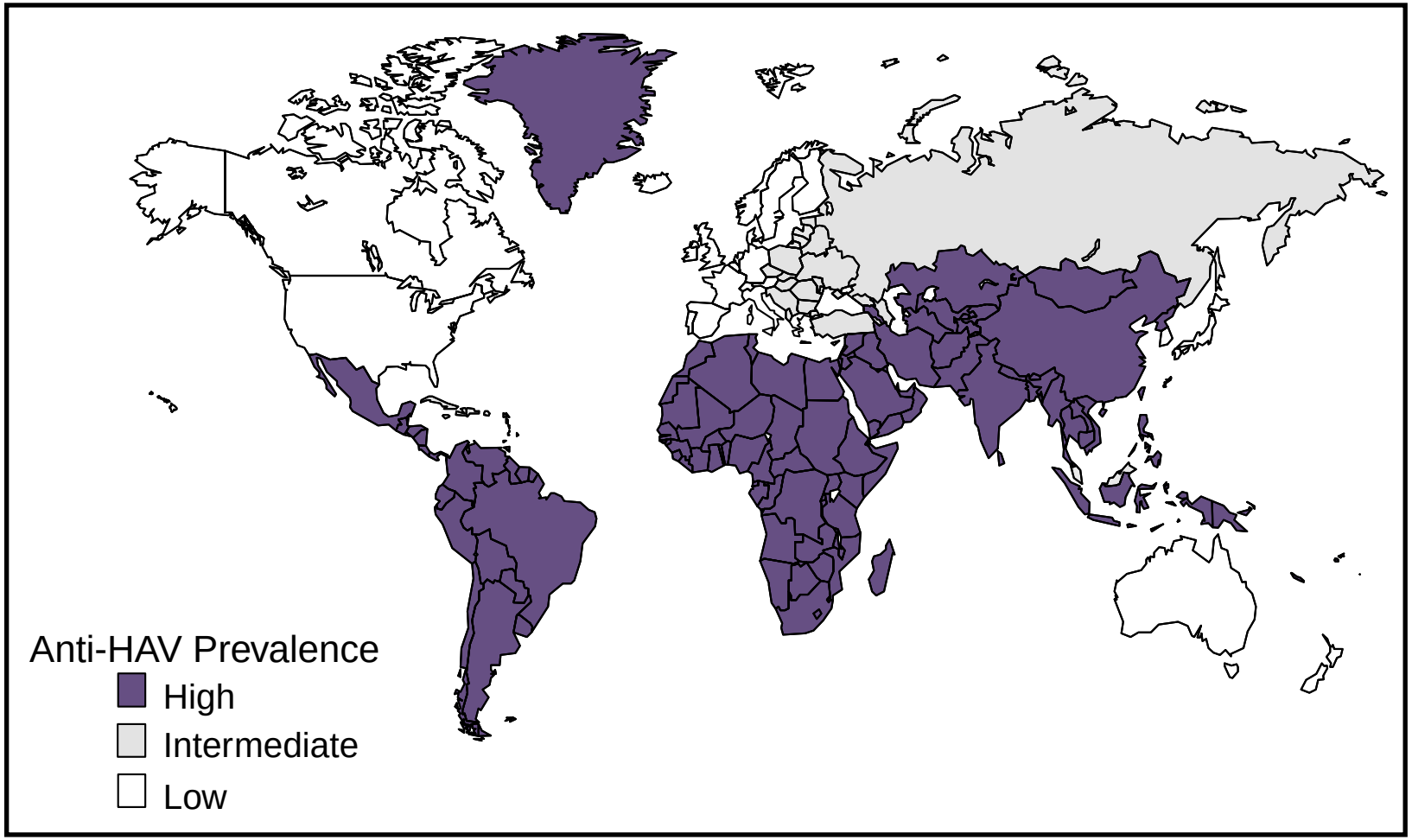
Occurrence

HAV is highly endemic throughout the developing world, but, in general, of low endemicity in developed countries (within developed countries there might be pockets of increased endemicity).

Risk for Travelers

The risk of acquiring HAV infection for U.S. residents traveling abroad varies with living conditions, length of stay, and the incidence of HAV in the area visited. HAV is **the most common vaccine-preventable disease in travelers** and HAV vaccine or immune globulin (IG), or both, is recommended for all susceptible people traveling to or working in countries with an intermediate or a high endemicity of infection (see Map 3-2). Travelers to North America (except Mexico),

Map 3-2.—Anti-HAV Prevalence, 2000.



Japan, Australia, New Zealand, and developed countries in Europe are at no greater risk of infection than in the United States. For travelers to developing countries, risk of infection increases with duration of travel and is highest for those who live in or visit rural areas, trek in back country areas, or frequently eat or drink in settings of poor sanitation. Nevertheless, many cases of travel-related HAV occur in travelers to developing countries with "standard" tourist itineraries, accommodations, and food consumption behaviors.

Preventive Measures

Vaccine

Two HAV vaccines are currently licensed in the United States: HAVRIX® (manufactured by GlaxoSmithKline) and VAQTA® (manufactured by Merck & Co., Inc). Both vaccines are made of inactivated virus adsorbed to aluminum hydroxide as an adjuvant. HAVRIX® is prepared with 2-phenoxyethanol as a preservative, while VAQTA® is formulated without a preservative. The vaccine should be administered by intramuscular injection in the deltoid muscle.

Both HAVRIX® and VAQTA® are currently licensed in two formulations, and the formulation and number of doses vary according to the recipient's age. For HAVRIX®, the schedule for anyone 2 through 18 years of age is two 720-enzyme-linked immunosorbent assay unit (EL.U.) doses, with the second dose given 6 to 12 months after the first. For anyone 19 years of age or older, the schedule is two 1,400-EL.U. doses, with the second dose given 6 to 12 months after the first (Table 3-4). For VAQTA®, the schedule for anyone 2 through 18 years of age is two 25-unit (U) doses, the second given 6 to 18 months after the first, and for anyone 19 years of age or older, the schedule is two 50-U doses given 6 months apart (Table 3-5).

Vaccination with the age-appropriate dose (see Tables 3-4 and 3-5) is preferred for anyone who plans to travel repeatedly or reside for long periods in high- or intermediate-risk areas. Studies have shown that protective antibody levels develop in 94% to 100% of those 19 years of age or older one month after the first dose of vaccine is given and protection can be assumed 4 weeks after receiving the first vaccine dose, although a second dose is necessary for long-term protection. Because protection might not be complete until 4 weeks after vaccine administration, anyone traveling to a high-risk area less than 4 weeks after the initial dose should also be given IG (0.02 milliliters per kilogram [mL/kg]) when available, but at a different injection site. Data on the long-term persistence of antibody after HAV vaccination are limited because the currently available vaccines have been under evaluation for only 5 to 7 years. Estimates of antibody persistence derived from kinetic models of antibody decline suggest that protective levels of anti-HAV could persist for at least 20 years.

Travelers younger than 2 years of age should receive a single dose of IG (0.02 mL/kg) because neither vaccine is licensed for infants. Travelers who are allergic to a vaccine component or otherwise elect not to receive vaccine should receive a single dose of IG (0.02 mL/kg), which provides effective protection against HAV for up to 3 months. For anyone traveling for longer than 3 months, an IG dose of 0.06 mL/kg should be given, and must be repeated if the duration of travel is longer than 5 months. (See Table 3-6 for approximate IG dosages.)

Table 3-4.—Recommended Doses of HAVRIX®*.

AGE GROUP (YEARS)	DOSE (EL.U.)§	VOLUME	NUMBER OF DOSES	SCHEDULE (MONTHS)
2 through 18	720	0.5 milliliter	2	0, 6 to 12
19 or older	1,440	1.0 milliliter	2	0, 6 to 12

*Hepatitis A vaccine, inactivated, GlaxoSmithKline.
§EL.U. = enzyme-linked immunosorbent assay (ELISA) units.

Table 3-5.—Recommended Doses of VAQTA®*.

AGE GROUP (YEARS)	DOSE	VOLUME	NUMBER OF DOSES	SCHEDULE (MONTHS)
2 through 18	25 units	0.5 milliliter	2	0, 6 to 18
19 or older	50 units	1.0 milliliter	2	0, 6

* Hepatitis A vaccine, inactivated, Merck & Co., Inc.

Table 3-6.—Immune Globulin for Protection Against Viral Hepatitis A.

LENGTH OF STAY	BODY WEIGHT		DOSE VOLUME*	COMMENTS
	Pounds	**Kilograms**		
Less than 3 months	Less than 50 50 to 100 More than 100	Less than 23 23 to 45 More than 45	0.5 milliliters 1.0 milliliters 2.0 milliliters	Dose volume depends on body weight and length of stay.
3 to 5 months	Less than 22 22 to 49 50 to 100 More than 100	Less than 10 10 to 22 23 to 45 More than 45	0.5 milliliters 1.0 milliliters 2.5 milliliters 5.0 milliliters	

*For intramuscular injection.

Although vaccination of an immune traveler is not contraindicated and does not increase the risk of adverse effects, screening for total antibodies to HAV (anti-HAV) before travel can be useful to determine susceptibility and eliminate unnecessary vaccination or IG prophylaxis of immune travelers. Such serologic screening for susceptibility might be indicated for adult travelers who are likely to have had prior HAV infection if the cost of screening (laboratory and office visit) is less than the cost of vaccination or IG prophylaxis and if testing will not interfere with subsequent receipt of vaccine or IG. Such travelers can include those older than 40 years of age and those born in parts of the world with intermediate or high endemicity (see Map 3-2). Postvaccination testing for serologic response is not indicated.

Adverse Reactions

Among those 19 years of age or older, the most frequently reported side effects occurring within 3 days following a dose of HAVRIX® were soreness at the injection site (56%), headache (14%), and malaise (7%). In clinical studies among those 18 years of age or younger, the most frequently reported side effects were soreness at the injection site (15%), feeding problems (8%), headache (4%), and injection-site induration (4%). Among those 19 years of age or older, the most frequent side effects occurring within 5 days following vaccination with VAQTA® were tenderness (53%), pain (51%), warmth at the injection site (17.3%), and headache (16.1%). Among those 18 years of age or younger, the most common side effects reported were pain (19%), tenderness (17%), and warmth at the injection site (9%).

Postlicensure reports, without regard to causality, of serious events received by the vaccine manufacturers have included (but might not have been limited to) anaphylaxis, Guillain-Barré syndrome, brachial plexus neuropathy, transverse myelitis, multiple sclerosis, encephalopathy, and erythema multiforme. Most of these events have occurred among adults, and many have occurred among people receiving other vaccines concurrently. For serious adverse events for which background incidence data were known, the rates for vaccine recipients were not higher than would be expected for an unvaccinated population.

Immune Globulin.—Immune globulin for intramuscular administration prepared in the United States has few side effects (primarily soreness at the injection site) and has never been shown to transmit infectious agents (hepatitis B virus [HBV], hepatitis C virus [HCV], or human immunodeficiency virus [HIV]). Since December 1994, all IG products commercially available in the United States have had to undergo a viral inactivation procedure or be negative for HCV ribonucleic acid (RNA) before release.

Precautions and Contraindications

Neither vaccine should be administered to travelers with a history of hypersensitivity to alum and HAVRIX® should not be administered to travelers with a history of hypersensitivity reactions to the preservative 2-phenoxyethanol. Because the vaccine is inactivated, no special precautions need to be taken for vaccination of immunocompromised travelers.

Pregnancy.—The safety of HAV vaccine for pregnant women has not been determined. However, because HAV vaccine is produced from inactivated HAV, the theoretical risk to either the pregnant woman or the developing fetus is thought to be very low. The risk of vaccination should be weighed against the risk of HAV in women travelers who might be at high risk for exposure to HAV. Pregnancy is not a contraindication to using immune globulin.

Other

HAV is inactivated by boiling or cooking food and beverage items to 85° Celsius (185° Fahrenheit) for at least one minute. Foods and beverages heated to this temperature and for this length of time cannot serve as vehicles for disease unless contaminated after heating. Adequate chlorination of water as recommended in the United States will inactivate HAV. Travelers should be advised that, to minimize their risk of HAV and other enteric diseases in developing countries, they should avoid potentially contaminated water or food. Travelers should also be advised to avoid drinking beverages (with or without ice) of unknown purity, and eating uncooked shellfish and uncooked fruits or vegetables that are not peeled or prepared by the traveler personally.

HEPATITIS, VIRAL, TYPE B

Description

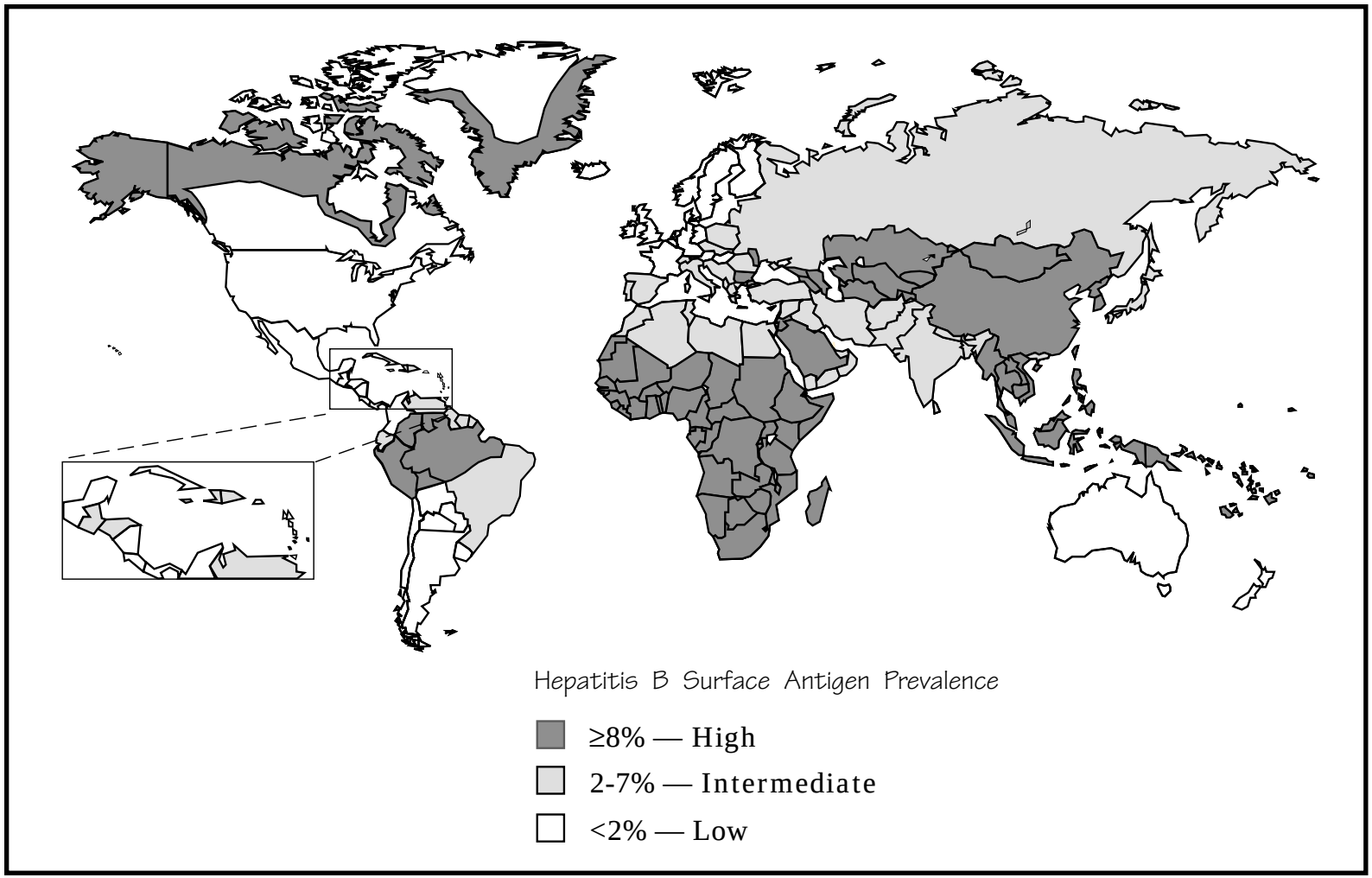
Hepatitis B is a viral infection with clinical manifestations that include anorexia, abdominal discomfort, nausea, and vomiting, and often progresses to jaundice. Severity ranges from inapparent infections detectable only by elevated liver function tests to fulminating, fatal cases of acute hepatic necrosis.

Hepatitis B virus (HBV) is transmitted primarily through activities that involve contact with blood or blood-derived fluids. The most frequent mode of transmission is through sexual activity, either heterosexual or homosexual, between an infected and a susceptible person. Principal activities that can result in blood exposure include working in health care fields (medical, dental, laboratory, or other) that entail direct exposure to human blood; receiving blood transfusions that have not been screened for HBV; and having dental, medical, or other exposure to needles (for example, acupuncture, tattooing, or injecting drug use) that are contaminated with HBV. In addition, open skin lesions in children or adults, due to factors such as impetigo, scabies, and scratched insect bites, can play a role in disease transmission if direct exposure to wound exudates occurs.

Occurrence

The prevalence of chronic HBV infection is high ($8%) in all socioeconomic groups in certain areas (see Map 3-3): all of Africa; Southeast Asia, including China, Korea, Indonesia, and the Philippines; the Middle East, except Israel; south and western Pacific islands; the interior Amazon River basin; and certain parts of the Caribbean (that is, Haiti and the Dominican Republic). The prevalence of chronic HBV infection is intermediate (2% to 7%) in south central and southwest Asia, Israel,

Map 3-3.—*Geographic Distribution of Hepatitis B Prevalence, 2000.*



Japan, eastern and southern Europe, Russia, most areas surrounding the Amazon River basin, Honduras, and Guatemala. In northern and western Europe, North America, Australia, New Zealand, Mexico, and southern South America, chronic HBV infection prevalence is low (<2%) in the general population.

Risk for Travelers

The risk of HBV infection for international travelers is generally low, except for certain travelers in countries with intermediate or high HBV endemicity. Factors to consider in assessing risk include (1) the prevalence of chronic HBV infection in the local population; (2) the extent of direct contact with blood or secretions, or of sexual contact with potentially infected people; and (3) the duration of travel.

Preventive Measures

Vaccine

HBV vaccination is currently recommended for all people who work in health care fields (medical, dental, laboratory, or other) that entail exposure to human blood. HBV vaccination should be considered for travelers who plan to reside for 6 months or longer in areas with intermediate to high levels of endemic HBV transmission (that is, with HBV surface antigen [HbsAg] prevalence $2%) and who will have any of the previously discussed types of contact with the local populations. In particular, travelers who anticipate sexual contact or who will have daily physical contact with the local population; or who are likely to seek medical, dental, or other treatment in local facilities; or any combination of these activities during their stay should be advised to receive the vaccine. Those who will be traveling for less than 6 months should also be vaccinated if they will have direct contact with blood, or sexual contact with residents of areas with intermediate to high levels of endemic HBV transmission.

Two types of HBV vaccines have been licensed in the United States. One, which was manufactured from the plasma of people with chronic HBV infection, is no longer produced in the United States. The remaining available type of vaccine is produced through recombinant deoxyribonucleic acid (DNA) technology by common baker's yeast into which the gene for HbsAg has been inserted. This type of HBV vaccine has been shown to be very safe when given to people of all ages.

The usual schedule of primary vaccination consists of three intramuscular doses of vaccine. The recommended dose varies by product and the recipient's age (Table 3-7). The vaccine is usually administered as a three-dose series on a 0-, 1-, and 6-month schedule. The second dose should be given 1 month after the first dose; the third dose should be given at least 2 months after the second does and at least 4 months after the first dose. Alternatively, the vaccine produced by GlaxoSmith-Kline licensed to be administered on a four-dose schedule at 0, 1, 2, and 12 months. There is also a two-dose schedule for a vaccine produced by Merck & Co., Inc. that has been licensed for children and adolescents 11 through 15 years of age. Using the two-dose schedule, the adult dose of Recombivax-HB® is administered, with the second dose given 4 to 6 months after the first dose.

Table 3-7.—Recommended Doses of Currently Licensed Hepatitis B Vaccines.

GROUP	DOSE	
	Recombivax-HB®*	**Engerix-B®***
All infants (regardless of mother's HBsAg status), children, adolescents, and adults, birth through 19 years of age.	5 µg	10 µg
Adults 20 years of age or older.†	10 µg	20 µg
Dialysis patients and other immunocompromised people.	40 µg§	40 µg¶

µg = microgram.
*Both vaccines are routinely administered in a three-dose series. Engerix-B® also has been licensed for a four-dose series administered at 0, 1, 2, and 12 months.
†Recombivax-HB® is now approved in a two-dose schedule for 11- through15-year-olds (see "Preventive Measures," this section, pages 93 and 94).
§Special formulation (40 µg in 1.0 milliliters).
¶Two 1.0 milliliter doses given at one site, in a four-dose schedule at 0, 1, 2, 6 months.

Vaccination should ideally begin at least 6 months before travel so the full vaccine series can be completed prior to departure. Because some protection is provided by one or two doses, the vaccine series should be initiated, if indicated, even if it cannot be completed prior to departure. However, optimal protection is not conferred until after the final vaccine dose. There is no evidence of interference between HBV vaccine and other simultaneously administered vaccine(s) or with immune globulin. The optimum site of injection in adults is the deltoid muscle; vaccination in the buttocks results in poorer antibody response. Long-term studies of healthy adults and children indicate that immunologic memory remains intact for at least 15 years and confers protection against chronic HBV infection, even though HBV surface antibody (anti-HBVs) levels can become low or decline below detectable levels. For children and adults whose immune status is normal, booster doses of vaccine are not recommended, nor is serologic testing to assess antibody levels necessary for most vaccinees. (See Chapter 1, "Vaccine Information," "Vaccine Recommendations for Infants and Children," pages 12 through 21, for a discussion of the HBV immunization schedule for infants who will be traveling.)

Adverse Reactions

Pain at the injection site (3% to 29%) and elevated temperature >37.7° Celsius (99.9° Fahrenheit) (1% to 6%) are the most frequently reported side effects among vaccine recipients. In placebo-controlled studies, these side effects were reported no more frequently among people receiving HBV vaccine than among people receiving placebo. Among children receiving both HBV vaccine and

diphtheria-tetanus-pertussis (DTP) vaccine, these mild side effects have been observed no more frequently than among children receiving DTP vaccine alone.

A low rate of anaphylaxis has been observed in vaccine recipients based on reports to the Vaccine Adverse Event Reporting System (VAERS) (with an estimated incidence of 1 case in 600,000 vaccine doses distributed); 2 anaphylaxis cases were in children. None of the people who developed anaphylaxis died; however, anaphylaxis can be fatal and HBV vaccine can, in very rare instances, cause a life-threatening hypersensitivity reaction in certain individuals. Therefore, further vaccination with HBV vaccine is contraindicated in people with a history of anaphylaxis after a previous dose of vaccine.

In the United States, surveillance of adverse events has shown a possible association between Guillain-Barré syndrome (GBS) and receipt of the first vaccine dose of plasma-derived HBV vaccine in adults. However, analysis of GBS reported to the Centers for Disease Control and Prevention (CDC), U.S. Food and Drug Administration (FDA), and vaccine manufacturers for the estimated 2.5 million adults who received one or more doses of recombinant HBV vaccine from 1986 to 1990 did not demonstrate an association between receipt of recombinant vaccine and GBS.

Case reports of other rare adverse events following HBV vaccination that have been published in the medical literature have included multiple sclerosis, optic neuritis, rheumatoid arthritis, type I diabetes, autoimmune disease, and alopecia. Most of these reported adverse events have been in adults and no studies have compared the frequency of occurrence of the purported vaccine-associated disease or syndrome with the frequency of occurrence in an unvaccinated population. Analysis of reports to the VAERS has not found an increased frequency of adverse events among children since implementation of routine infant HBV vaccination.

Any presumed risk of adverse events associated with HBV vaccination must be balanced with the expected 5,000 deaths from HBV-related liver disease that would occur in the United States each year without immunization, assuming a 5% lifetime risk of HBV infection. Surveillance for vaccine-associated adverse events will continue to be an important part of HBV vaccination programs in spite of the current record of safety.

Precautions and Contraindications

On the basis of limited data, there is no apparent risk of adverse events to the developing fetus when HBV vaccine is administered to pregnant women. The vaccine contains noninfectious HBsAg particles and should cause no risk to the fetus. HBV infection affecting a pregnant woman can result in serious disease for the mother and chronic infection for the newborn. Therefore, neither pregnancy nor lactation should be considered a contraindication for vaccination.

Other

Behavioral preventive measures are similar to those for human immunodeficiency virus and acquired immunodeficiency syndrome (see “Acquired Immunodeficiency Syndrome (AIDS),” this chapter, pages 57 through 59).

HEPATITIS, VIRAL, TYPE C

Description

Hepatitis C is a liver disease caused by the hepatitis C virus (HCV), which is found in the blood of infected people. Most people who acquire HCV infection either have no symptoms or have a mild clinical illness. However, chronic HCV develops in most (75% to 85%) people, with active liver disease developing in 60% to 70% of chronically infected people.

HCV is transmitted primarily through activities that result in the exchange of blood; it is less commonly transmitted by sexual activity. The most frequent mode of transmission in the United States is through sharing of drug-injecting equipment among injecting drug users. For international travelers, the principal activities that can result in blood exposure include receiving blood transfusions that have not been screened for HCV; having medical or dental procedures or engaging in activities (for example, acupuncture, tattooing, or injecting drug use) in which equipment has not been adequately sterilized or disinfected or in which contaminated equipment is reused; and working in health care fields (for example, medical, dental, or laboratory) that entail direct exposure to human blood.

Occurrence

HCV is endemic in most areas of the world, with approximately 3% (170 million) of the world's population infected with HCV. For many countries in the world, no reliable data exist on the prevalence of HCV infection. Using available data from seroprevalence studies among blood donors, HCV prevalence is highest (17% to 26%) in Egypt. HCV prevalence is intermediate (1% to 5%) in eastern Europe, the Mediterranean, the Middle East, the Indian subcontinent, parts of Africa, and Asia. HCV prevalence is low (0.2% to 0.5%) in western Europe; North America; most areas of Central America; Australia; and limited regions of Africa, including South Africa. HCV prevalence is lowest (0.01% to 0.10%) in the United Kingdom and Scandinavia.

Risk for Travelers

Travelers' risk for contracting HCV infection is generally low. The major factor travelers should be advised to consider in assessing risk is the extent of their direct contact with blood, particularly receipt of blood transfusions from unscreened donors, or exposure to contaminated equipment used in health care-related or cosmetic (for example, tattooing) procedures.

Preventive Measures

No vaccine is available. When seeking medical or dental care, travelers should be advised to be alert to the use of medical, surgical, and dental equipment that has not been adequately sterilized or disinfected, reuse of contaminated equipment, and unsafe injecting practices (for example, reuse of disposable needles and syringes). Travelers should be advised to consider the health risks if they are

thinking about getting a tattoo or body piercing. HCV (and other blood-borne pathogens) can be transmitted if the tools that are used are not sterile or if the artist or piercer does not follow other proper infection-control procedures (for example, washing hands, using latex gloves, and cleaning and disinfecting surfaces and instruments). (See "Acquired Immunodeficiency Syndrome (AIDS)," this chapter, pages 57 through 59.)

HEPATITIS, VIRAL, TYPE E

Description

Hepatitis E is an enterically transmitted viral disease that can be distinguished from other forms of acute viral hepatitis only by using specific seriological testing, the availability of which is limited at this time. Disease occurs primarily in adults. A low (0.5% to 4.0%) case fatality rate is associated with hepatitis E in the general population, but among pregnant women mortality has ranged from 17% to 33%; the highest rates of fulminant hepatitis and death have occurred during the third trimester. No chronic infection after initial hepatitis E infection has been documented.

Hepatitis E virus (HEV) is transmitted by the fecal-oral route. HEV occurs both in epidemic and sporadic forms and is associated primarily with the ingestion of fecally contaminated drinking water. The potential for HEV transmission from contaminated food is still under investigation, and there is no evidence of transmission by percutaneous or sexual exposures.

Occurrence

Epidemics and sporadic cases of HEV have been reported from areas of Asia (Afghanistan, Bangladesh, Burma (Myanmar), China, India, Indonesia, Kazakhstan, Kyrgyzstan, Malaysia, Mongolia, Nepal, Pakistan, Tajikistan, Turkmenistan, and Uzbekistan), Mexico, the Middle East, northern Africa, and sub-Saharan Africa. Outbreaks have not been recognized in Europe, the United States, Australia, or South America. Several imported cases of HEV have been identified in American travelers and two cases have been identified in patients with no history of international travel; studies are in progress to determine if HEV is an endemic disease in the United States.

Risk for Travelers

Travelers to developing countries where HEV occurs can be at risk of acquiring this disease through contaminated water.

Preventive Measures

There is no vaccine to prevent HEV. Immune globulin (IG) prepared from plasma collected in HEV endemic areas has not been effective in preventing clinical disease during HEV outbreaks. IG prepared from plasma collected from parts of the world where HEV is not an endemic disease is

unlikely to be effective. The best prevention of infection is to avoid potentially contaminated water (and food), as with hepatitis A and other enteric infections.

INFLUENZA

Description

Influenzas A and B are the major types of influenza viruses that cause human respiratory disease. Influenza A viruses are further classified into subtypes on the basis of two surface antigens: hemagglutinin (H) and neuraminidase (N). Although both influenza A and B viruses undergo continual antigenic change (that is, antigenic drift), influenza B viruses undergo antigenic change more slowly and are not divided into subtypes. Since 1977, influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation.

Occurrence

Epidemics of influenza generally occur during the winter months on an annual or near annual basis and are responsible for an average of approximately 20,000 deaths in the United States each year. Influenza virus infections cause disease in all age groups. Rates of infection are highest among infants, children, and adolescents, but rates of serious morbidity and mortality are highest among people 50 years of age or older and people of any age who have medical conditions that place them at high risk for complications from influenza. Influenza viruses also can cause global epidemics of disease, known as pandemics, during which rates of morbidity and mortality from influenza-related complications can increase dramatically.

Risk for Travelers

The risk for exposure to influenza during international travel varies depending on the time of year and destination. In the tropics, influenza can occur throughout the year, while most activity occurs from April through September in the temperate regions of the Southern Hemisphere. In temperate climates, travelers can also be exposed to influenza during the summer, especially when traveling as part of large tourist groups with travelers from areas of the world where influenza viruses are circulating. Travelers at high risk for complications of influenza should be advised to consider receiving influenza vaccine before travel if (1) influenza vaccine was not received during the preceding fall or winter, (2) travel is planned to the tropics, (3) travel is planned with large groups of tourists at any time of year, or (4) travel is planned to the Southern Hemisphere from April through September. Travelers at high risk who received the previous season's vaccine before travel should be revaccinated in the fall or winter with the current vaccine.

Because influenza vaccine might not be available during the summer in North America, travelers 50 years of age or older and others at high risk for influenza-related complications who plan summer travel might be advised to consult with their physicians to discuss the symptoms and risks of influenza before embarking on their travel.

Preventive Measures

Vaccine

In the United States, the main option for reducing the impact of influenza is immunoprophylaxis with inactivated (that is, killed-virus) vaccine. In addition, the use of influenza-specific antiviral drugs for chemoprophylaxis or therapy of influenza are important adjuncts to vaccine. Annual vaccination of people at high risk for complications before the influenza season is the most effective measure for reducing the impact. Vaccine is recommended for all travelers, and particularly for the following groups who are at risk for complications from influenza:

- People 50 years of age or older. (In 2000, the 50- through 64-years-of-age group was added to those recommended for annual vaccination because a substantial proportion of them have a medical condition that places them at increased risk of influenza-related complications.)

- Residents of nursing homes and other chronic-care facilities that house people of any age who have chronic medical conditions.

- Anyone 6 months of age or older who has chronic disorders of the pulmonary or cardiovascular systems, including asthma.

- Anyone 6 months of age or older who has required regular medical followup or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications, human immunodeficiency virus [HIV], or acquired immunodeficiency syndrome [AIDS]).

- Anyone 6 months to 18 years of age who is receiving long-term aspirin therapy and, therefore, might be at risk for developing Reye's syndrome after influenza.

- Women who will be in the second or third trimester of pregnancy during the influenza season.

Dosing, Route, and Timing of Vaccination

Even when current influenza vaccine contains one or more of the antigens administered in previous years, annual vaccination with the current vaccine is necessary because immunity declines during the year after vaccination. Dosage recommendations differ according to age group. Two doses administered at least one month apart may be required for satisfactory antibody responses among previously unvaccinated infants and children younger than 9 years of age. The second dose should be administered before December, if possible. In adults, studies have indicated little or no improvement in antibody response when a second dose is administered during the same season.

The intramuscular route is recommended for influenza vaccine. Infants and young children should be vaccinated in the anterolateral aspect of the thigh; all other vaccine recipients should be vaccinated in the deltoid muscle.

Composition of the Vaccine

Influenza vaccine contains three strains of inactivated influenza viruses. These viruses are updated annually and are representative of viruses likely to circulate in the upcoming season. Because the vaccine is grown in hen eggs, the vaccine might contain small amounts of egg protein. Influenza vaccine distributed in the United States might also contain thimerosal, a mercury-containing preservative. Manufacturing processes differ by manufacturer and the package insert should be consulted regarding the use of other compounds to inactivate the viruses or limit bacterial contamination.

Adverse Reactions

Inactivated influenza vaccine contains noninfectious viruses and cannot cause influenza. Respiratory disease after vaccination represents coincidental illness unrelated to influenza vaccination.

Local Reactions.—The most frequent side effect of vaccination is soreness at the vaccination site that lasts up to 2 days. These local reactions generally are mild and rarely interfere with the ability to conduct usual daily activities.

Systemic Reactions.—Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect people who have had no previous exposure to the influenza virus antigens in the vaccine (for example, young children). These reactions begin 6 to 12 hours after vaccination and can persist for 1 to 2 days.

Immediate—presumably allergic—reactions (for example, hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; most reactions likely are caused by residual egg protein and occur among people who have severe egg allergy. People who have developed hives, have had swelling of the lips or tongue, or have experienced acute respiratory distress or collapse after eating eggs should be advised to consult a physician for appropriate evaluation to help determine if vaccine should be administered. People who have documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs—including those who have had occupational asthma or other allergic responses due to exposure to egg protein—might also be at increased risk for reactions from influenza vaccine, and similar consultation should be advised. Protocols have been published for safely administering influenza vaccine to people with egg allergies.

Guillain-Barré Syndrome (GBS).—Investigations to date suggest that there is no large increase in GBS associated with influenza vaccines (other than the "swine flu" vaccine) and that if influenza vaccine does pose a risk it is probably quite small—on the order of 1 to 2 episodes per million

people vaccinated. There are case reports of GBS following influenza, but no epidemiologic studies documenting such an association.

Precautions and Contraindications

The target groups for influenza and pneumococcal vaccination overlap considerably. For travelers at high risk who have not previously been vaccinated with pneumococcal vaccine, health care providers should strongly consider administering pneumococcal and influenza vaccines concurrently. Both vaccines can be administered at the same time at different sites without increasing side effects. However, influenza vaccine is administered each year, while pneumococcal vaccine is not. Infants and children at high risk for influenza-related complications can receive influenza vaccine at the same time they receive other routine vaccinations.

Pregnancy.—Because currently available influenza vaccine is an inactivated vaccine, many experts consider influenza vaccination safe during any stage of pregnancy. A study of influenza vaccination of more than 2,000 pregnant women demonstrated no adverse fetal effects associated with influenza vaccine. However, more data are needed. Some experts prefer to administer influenza vaccine during the second trimester to avoid a coincidental association with spontaneous abortion, which is common in the first trimester, and because exposures to vaccines have traditionally been avoided during this time. Influenza vaccine does not affect the safety of mothers who are breast-feeding or their infants. Breast-feeding does not adversely affect immune response and is not a contraindication for vaccination.

People Infected With Human Immunodeficiency Virus (HIV).—Limited information exists regarding the frequency and severity of influenza illness or the benefits of influenza vaccination among HIV-infected people. Influenza vaccine has produced protective influenza antibody titers and has been shown to prevent influenza in HIV-infected people who have minimal AIDS-related symptoms and high CD4+ T-lymphocyte cell counts. However, in people who have advanced HIV disease and low CD4+ T-lymphocyte cell counts, influenza vaccine might not induce protective antibody titers; a second dose of vaccine does not improve the immune response in these people. Deterioration of CD4+ T-lymphocyte cell counts and progression of HIV disease have not been demonstrated among HIV-infected people who receive the vaccine. The effect of antiretroviral therapy on potential increases in HIV ribonucleic acid (RNA) levels following either natural influenza infection or influenza vaccine is unknown. Because influenza can result in serious illness and complications and because influenza vaccination can result in the production of protective antibody titers, vaccination will benefit many HIV-infected people, including HIV-infected pregnant women.

Other

Antiviral drugs for influenza are an important adjunct to influenza vaccine for the control and prevention of influenza. The four currently licensed U.S. agents are amantadine, rimantadine, zanamivir, and oseltamivir. Amantadine and rimantadine have specific activity again influenza A viruses but not influenza B viruses. Both are approved by the U.S. Food and Drug Administration for the treatment and prophylaxis of influenza A virus infections. Zanamivir and oseltamivir have

activity against both influenzas A and B. Both drugs are currently approved for treatment, though only oseltamivir has been approved for prophylaxis. These four drugs differ in terms of dosing, approved age groups for use, side effects, and cost. The package inserts should be consulted for more information.

LASSA FEVER

Description

Lassa fever is a severe, often fatal, hemorrhagic fever that is caused by a virus transmitted from asymptomatically infected rodent reservoirs to humans.

Occurrence

This illness is limited to rural areas of west Africa with hyperendemic areas in eastern Sierra Leone, Liberia, and Nigeria. Periodomestic exposure to infected rodents is the most likely source of infection. Transmission to humans can occur via inhalation of primary aerosols from rodent urine or by ingestion of contaminated food. Rodent infestation and inappropriate food storage enhance human infection. Person-to-person transmission of Lassa fever has also been described, most notably in the hospital setting.

Risk for Travelers

The risk of infection in international travelers is considered small. Only a few cases (one recent) were confirmed in international travelers staying or living in traditional habitations in the countryside or in small villages. There is no risk for travelers staying in hotels and having no contact with rodents or patients at home or in a health center. Medical personnel and relief workers involved in the close management of patients and relief workers in endemic areas should be aware of the risk of nosocomial transmission.

Preventive Measures

No vaccine is currently available. Strict barrier nursing precautions (use of gloves, gowns, masks, and goggles to prevent direct contact between medical personnel and patients or patient secretions, excretions, or biological samples) are recommended to avoid nosocomial infections. Travelers should be advised to avoid contact with rodents in endemic areas.

Treatment

Treatment with the antiviral drug ribavirin can be life saving if started early.

LEISHMANIASIS

Description

Leishmaniasis is a parasitic disease transmitted by the bite of some species of sand flies. The disease most commonly manifests either in a cutaneous (skin) form or in a visceral (internal organ) form. Cutaneous leishmaniasis is characterized by one or more skin sores (either open or closed) that develop weeks to months after a person is bitten by infected sand flies. The manifestations of visceral leishmaniasis, such as fever, enlargement of the spleen and liver, and anemia, typically develop months, but sometimes years, after a person becomes infected.

Occurrence

Leishmaniasis is found in approximately 90 tropical and subtropical countries around the world. More than 90% of the world's cases of visceral leishmaniasis occur in Bangladesh, Brazil, India, Nepal, and Sudan. It also occurs in some of the following regions: the Americas (from northern Argentina to southern Texas in the United States); northern Asia; the Middle East; and Africa (particularly east and north Africa). Leishmaniasis is not found in Australia or Oceania (that is, the Pacific islands, including Melanesia, Micronesia, and Polynesia).

Risk for Travelers

People of all ages are at risk for leishmaniasis if they live or travel where leishmaniasis is found. Leishmaniasis usually is more common in rural than urban areas, but it is found in the outskirts of some cities. Risk is highest for people who are outdoors in leishmaniasis-endemic areas between dusk and dawn. Adventure travelers, Peace Corps volunteers, missionaries, ornithologists, other people who do research outdoors at night, and soldiers are examples of people who might have an increased risk for leishmaniasis (especially cutaneous leishmaniasis).

Preventive Measures

Vaccines and drugs for preventing infections are not currently available. Preventive measures for the individual traveler are aimed at reducing contact with sand flies. Travelers should be advised to avoid outdoor activities when sand flies are most active (dusk to dawn). Although sand flies are primarily nighttime biters, infection can be acquired during the daytime if resting sand flies are disturbed. Sand fly activity in an area can easily be underestimated because sand flies are noiseless fliers, and rare bites might not be noticed.

Travelers should be advised to use protective clothing and insect repellent for supplementary protection. Clothing should cover as much of the body as possible and tolerable in the climate. Repellent with N,N-diethylmetatoluamide (DEET) should be applied to exposed skin and under the edges of clothing, such as under the ends of sleeves and pant legs. It should be applied according to the manufacturer's instructions; repeated applications may be necessary under conditions of excessive

perspiration, wiping, and washing (see Chapter 4, "Health Hints for the International Traveler," "Repellents," pages 164 and 165). Although impregnation of clothing with permethrin can provide additional protection, it does not eliminate the need for repellent on exposed skin and should be repeated after every five washings.

Contact with sand flies can be reduced by using bed nets and screening on doors and windows. Fine-mesh netting (at least 18 holes to the linear inch; some sources advise even finer) is required for an effective barrier against sand flies, which are about one-third the size of mosquitoes. However, such closely woven bed nets might be difficult to tolerate in hot climates. Impregnating bed nets and window screens with permethrin aerosol can provide some protection, as can spraying dwellings with insecticides.

Treatment

Specific treatment is available and travelers should be advised to consult with an infectious disease or tropical medicine specialist.

LEPTOSPIROSIS

Description

Leptospirosis is a widespread zoonosis that is endemic worldwide, with a higher incidence in tropical climates, and infects a variety of wild and domestic animals that excrete the organism in their urine or in the fluids of parturition. Human infection occurs through exposure to water or soil contaminated by infected animals and has been associated with canoeing, kayaking, wading, and swimming in contaminated, untreated open water. The acute generalized illness associated with infection can mimic other tropical diseases (for example, dengue fever, malaria, and typhus), and common symptoms include fever, chills, myalgia, nausea, diarrhea, cough, and conjunctival suffusion. Manifestations of severe disease can include jaundice, renal failure, hemorrhage, pneumonitis, and hemodynamic collapse. The laboratory diagnosis of leptospirosis requires culture of the organism or demonstration of serologic conversion using the microagglutination test (MAT). However, culture is relatively insensitive and requires specialized media, and the MAT is difficult to perform and requires expertise. Therefore, availability of these techniques has been restricted to reference laboratories. Recently, several rapid and simple serologic tests have been developed that are reliable and commercially available.

Occurrence

Leptospira proliferate in fresh water, damp soil, vegetation, and mud. The occurrence of flooding after heavy rainfall facilitates the spread of the organism because, as water saturates the environment, *leptospira* present in the soil pass directly into surface waters. *Leptospira* can enter the body through

cut or abraded skin, mucous membranes, and conjunctivae. Ingestion of contaminated water can also lead to infection.

Risk to Travelers

Travelers participating in recreational water activities, such as white water rafting, adventure racing, or kayaking, in areas where leptospirosis is endemic or epidemic could be at increased risk for the disease, particularly during periods of flooding. Travelers who might be at increased risk for leptospirosis and who develop febrile illness should be advised to consider leptospirosis as one possible cause and to seek appropriate medical care.

Preventive Measures

There is no vaccine available to prevent leptospirosis. Travelers who might be at an increased risk for the disease should be advised to consider preventive measures such as wearing protective clothing and minimizing contact with potentially contaminated water. Such travelers also might benefit from chemoprophylaxis. Until further data become available, the Centers for Disease Control and Prevention recommends that travelers who might be at increased risk for leptospirosis be advised to consider chemoprophylaxis with doxycycline (200 milligrams orally, once a week), begun 1 to 2 days before exposure and continuing through the period of exposure.

Treatment

Treatment with antimicrobial agents (for example, penicillin, amoxicillin, or doxycycline) should be initiated early in the course of the disease, and intravenous antibiotics should be used for travelers with severe manifestations.

LYME DISEASE

Description

Lyme disease results from infection with spirochetes belonging to the *Borrelia burgdorferi* sensu lato complex. In Europe and Asia, most cases of Lyme disease are caused by *B. burgdorferi* sensu stricto, *B. afzelii*, or *B. garinii*; however, in the United States, all cases are caused by *B. burgdorferi* sensu stricto. The spirochetes are transmitted to humans through the bite of infected ticks of the *Ixodes ricinus* complex. Manifestations of Lyme disease include a characteristic expanding rash called erythema chronicum migrans at the site of tick attachment; fever; arthritis; and neurologic manifestations, including facial palsy.

Occurrence

Lyme disease occurs in temperate forested regions of Europe and Asia and in the northeastern, north central, and Pacific coastal regions of North America. It is not transmitted in the tropics.

Risk for Travelers

Travelers to endemic areas who have frequent or prolonged exposure to tick habitats could be at increased risk of Lyme disease.

Preventive Measures

Vaccine

A safe and efficacious vaccine is available for protection from Lyme disease in endemic areas of the United States. However, because of the genospecies diversity of the agents that cause Lyme disease in Europe and Asia, the vaccine is not likely to be highly efficacious outside North America. Recommendations for vaccine use by travelers to high-risk areas of the United States are available on the Internet at http://www.cdc.gov/ncidod/dvbid/lymeinfo.htm.

Other

Travelers to endemic areas should be advised to avoid tick habitats if possible. If exposure to tick habitats cannot be avoided, the application of repellents to skin and acaricides to clothing, as well as regular daily checks for any attached ticks can reduce the risk of infection. Because transmission of *B. burgdorferi* is unlikely to occur in the first 36 hours of tick attachment, prompt removal of any attached ticks will help prevent infection.

Treatment

Travelers who develop erythema chronicum migrans or other manifestations of Lyme disease should be advised to seek early medical attention. Lyme disease can usually be cured by an appropriate course of antibiotic treatment.

MALARIA

Description

Malaria in humans is caused by one of four protozoan species of the genus *Plasmodium: P. falciparum, P. vivax, P. ovale,* or *P. malariae.* All are transmitted by the bite of an infected female *Anopheles* mosquito. Occasionally, transmission occurs by blood transfusion or congenitally from mother to fetus. The disease is characterized by fever and influenza-like symptoms, including chills,

headache, myalgias, and malaise; these symptoms can occur at intervals. Malaria can be associated with anemia and jaundice, and *P. falciparum* infections can cause kidney failure, coma, and death. However, deaths from malaria are preventable.

Occurrence

Malaria is a major international public health problem, causing 300 to 500 million infections worldwide and several million deaths annually. Information on malaria risk in specific countries (Chapter 2, "Yellow Fever Vaccine Requirements and Information on Malaria Risk and Chloroquine Resistance, by Country," pages 23 through 54) is derived from various sources, including the World Health Organization. The information presented herein was accurate at the time of publication; however, factors that can vary from year to year, such as local weather conditions, mosquito vector density, and prevalence of infection, can have a marked effect on local malaria transmission patterns.

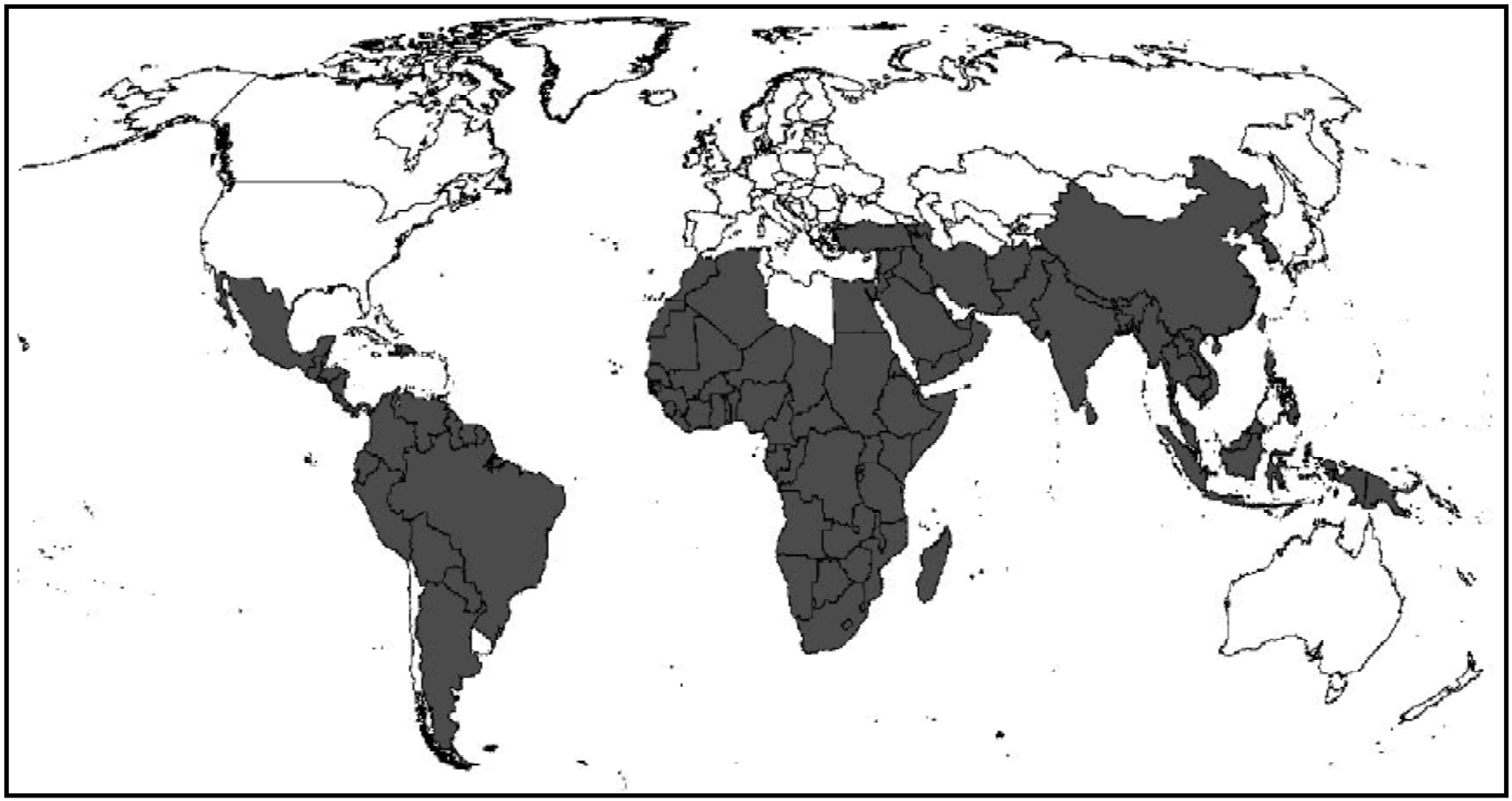
Risk for Travelers

Malaria transmission occurs in large areas of Central and South America, Hispaniola, sub-Saharan Africa, the Indian subcontinent, Southeast Asia, the Middle East, and Oceania (see Map 3-4). The estimated risk of a traveler's acquiring malaria varies markedly from area to area. This variability is a function of the intensity of transmission within the various regions and of the itinerary and time and type of travel. From 1985 through 1998, 3,555 cases of *P. falciparum* among U.S. civilians were reported to the Centers for Disease Control and Prevention (CDC). Of these, 3,007 (84%) were acquired in sub-Saharan Africa; 236 (7%) in Asia; 206 (6%) in the Caribbean and Central or South America; and 106 (3%) in other parts of the world. During this period, there were 47 fatal malaria infections among U.S. civilians; 46 (98%) were caused by *P. falciparum*, of which 36 (78%) were acquired in sub-Saharan Africa.

Thus, most imported *P. falciparum* malaria among American travelers was acquired in Africa south of the Sahara, even though only 508,000 U.S. residents traveled to countries in that region in 1998. In contrast, 25 million U.S. residents traveled from the United States that year to other countries with malaria (including 18 million travelers to Mexico). This disparity in the risk of acquiring malaria reflects the fact that the predominant species of malaria transmitted in sub-Saharan Africa is *P. falciparum*, that malaria transmission is generally higher in Africa than in other parts of the world, and that malaria is often transmitted in urban areas as well as rural areas in sub-Saharan Africa. In contrast, malaria transmission in general is lower in Asia and South America, a larger proportion of the malaria is *P. vivax*, and most urban areas do not have malaria transmission.

Estimating the risk of infection for different categories of travelers is difficult and can be significantly different even for people who travel or reside temporarily in the same general areas within a country. For example, travelers staying in air-conditioned hotels might be at lower risk than backpackers or adventure travelers. Similarly, long-term residents living in screened and air-conditioned housing are less likely to be exposed than are people living without such amenities, such as Peace Corps volunteers.

Map 3-4.—Malaria Endemic Countries, 2000.



Countries with Malaria Risk Countries with No Malaria Risk

Check the Yellow Pages for country specific information on prophylaxis.

Preventive Measures

No vaccine is currently available. However, all travelers to malarious areas of the world should be advised to use an appropriate drug regimen and personal protection measures to prevent malaria; however, travelers should be informed that, regardless of methods employed, malaria still can be contracted. Malaria symptoms can develop as early as 6 days after initial exposure in a malaria-endemic area and as late as several months after departure from a malarious area, after chemoprophylaxis has been terminated. Travelers should be advised that malaria can be treated effectively early in the course of the disease, but that delay of appropriate therapy can have serious or even fatal consequences. Travelers who have symptoms of malaria should be advised to seek prompt medical evaluation, including thick and thin blood smears, *as soon as possible*.

The resistance of *P. falciparum* to chloroquine has been confirmed in all areas with *P. falciparum* malaria except the Dominican Republic, Haiti, Central America west of the former Panama Canal Zone, Egypt, and some countries in the Middle East. In addition, resistance to both chloroquine and Fansidar® is widespread in Thailand; Burma (Myanmar); Cambodia; the Amazon River basin area of South America; and, increasingly, parts of east Africa. Resistance to mefloquine has been confirmed on the borders of Thailand with Burma (Myanmar) and Cambodia, in the western provinces of Cambodia, and in the eastern states of Burma (Myanmar).

Personal Protection Measures

Because of the nocturnal feeding habits of *Anopheles* mosquitoes, malaria transmission occurs primarily between dusk and dawn. Travelers should be advised to take protective measures to reduce contact with mosquitoes, especially during these hours. Such measures include remaining in well-screened areas, using mosquito nets, and wearing clothes that cover most of the body. Additionally, travelers should be advised to purchase insect repellent before travel for use on exposed skin. The most effective repellents contain N,N-diethylmetatoluamide (DEET), an ingredient in many commercially available insect repellents. The actual concentration of DEET varies among repellents and can be as high as 95%. Repellents with DEET concentrations of 30% to 35% are quite effective, and the effects should last for about 4 hours. Long-acting DEET products are now commercially available. Rarely, children exposed to DEET have had toxic encephalopathy. Travelers should be advised that the possibility of adverse reactions to DEET will be minimized if they take the following precautions: (1) apply repellent sparingly and only to exposed skin or clothing; (2) avoid applying high-concentration products to the skin; (3) avoid inhaling or ingesting repellents or getting them in the eyes; (4) avoid applying repellents to portions of children's hands that are likely to have contact with the eyes or mouth; (5) never use repellents on wounds or irritated skin; and (6) wash repellent-treated skin after coming indoors. If a reaction to insect repellent is suspected, travelers should be advised to wash treated skin and seek medical attention.

Travelers who will not be staying in well-screened or air-conditioned rooms should be advised to use a pyrethroid-containing flying-insect spray in living and sleeping areas during evening and nighttime hours. In addition, they should take additional precautions, including sleeping under mosquito netting (that is, bed nets). Permethrin (Permanone®) may be sprayed on clothing and bed

Checklist for Travelers to Malarious Areas

The following is a checklist of key issues to be considered in advising travelers. The numbers in parentheses refer to pages in the text where these issues are discussed in detail.

Risk of Malaria (pages 23 through 54)
Travelers should be informed about the risk of malaria infection and the presence of drug-resistant *Plasmodium falciparum* malaria in their areas of destination.

Personal Protective Measures (pages 163 through 165)
Travelers should be advised how to protect themselves against mosquito bites.

Chemoprophylaxis (pages 111 through 117)
Travelers should be:

- **!** Advised to start chemoprophylaxis before travel, and to use prophylaxis continuously while in malaria-endemic areas and for 4 weeks (chloroquine, mefloquine, and doxycycline) or 7 days (Malarone™) after leaving such areas.
- **!** Questioned about drug allergies and other contraindications for use of drugs to prevent malaria.
- **!** Advised which drug to use for chemoprophylaxis and, if appropriate, whether Fansidar® or Malarone™ should be carried for presumptive self-treatment.
- **!** Informed that any antimalarial drug can cause side effects and, if these side effects are serious, that medical help should be sought promptly and use of the drug discontinued.
- **!** Warned that they could acquire malaria even if they use malaria chemoprophylaxis.

In Case of Illness, travelers should be:

- **!** Informed that symptoms of malaria can be mild, and that they should suspect malaria if they experience fever or other symptoms such as persistent headaches, muscular aching and weakness, vomiting, or diarrhea.
- **!** Informed that malaria can be fatal if treatment is delayed. Medical help should be sought promptly if malaria is suspected, and a blood sample should be taken and examined for malaria parasites on one or more occasions.
- **!** Reminded that self-treatment should be taken only if prompt medical care is not available and that medical advice should still be sought as soon as possible after self-treatment.

Special Categories (pages 112 through 117, and 218)
Pregnant women and young children require special attention because of the potential effects of malaria illness and their inability to use some drugs (for example, doxycycline).

* * *

Adapted from International Travel and Health,
World Health Organization, Geneva, 1995

nets for additional protection against mosquitoes. Bed nets are more effective if they are treated with permethrin or deltamethrin insecticides. In the United States, permethrin spray or liquid can be used, or bed nets may be purchased that have already been impregnated. Permethrin or deltamethrin liquid may also be purchased overseas for the treatment of bed nets.

Chemoprophylaxis

In choosing an appropriate chemoprophylactic regimen before travel, the traveler and his or her health care provider should consider several factors. The travel itinerary should be reviewed in detail and compared with the information on areas of risk within a given country (Chapter 2, "Yellow Fever Vaccine Requirements and Information on Malaria Risk and Chloroquine Resistance, by Country," pages 23 though 54) to determine whether the traveler will actually be at risk of acquiring malaria. Whether the traveler will be at risk of acquiring drug-resistant *P. falciparum* malaria should also be determined. In addition, it should be established whether the traveler has previously experienced an allergic or other reaction to one of the antimalarial drugs of choice and whether medical care will be readily accessible during travel.

Malaria chemoprophylaxis with mefloquine or chloroquine should begin 1 to 2 weeks before travel to malarious areas (except for doxycycline or Malarone™, which can begin 1 to 2 days before travel). This allows for antimalarial drug to be in the blood prior to exposure, as well as for any potential side effects to be evaluated and treated before the traveler's departure. Chemoprophylaxis should continue during travel in the malarious areas and after leaving the malarious areas (4 weeks after travel for chloroquine, mefloquine, and doxycycline, and 7 days after travel for Malarone™). Drugs with longer half-lives (that are taken weekly) offer the advantage that they might have a wider margin of error if the traveler is late with a dose than drugs with short half-lives (that are taken daily). For example, if a traveler is 1 to 2 days late with a weekly drug, prophylactic blood levels can remain adequate; if they are 1 to 2 days late with a daily drug, protective blood levels are less likely to be maintained.

Travel to Areas <u>Without</u> Chloroquine-Resistant P. falciparum

For travel to areas of risk where chloroquine-resistant *P. falciparum* has NOT been reported, once-a-week use of chloroquine alone should be recommended. Chloroquine is usually well tolerated. The few people who experience uncomfortable side effects might tolerate the drug better by taking it with meals or in divided twice-a-week doses. As an alternative, the related compound hydroxy-chloroquine might be better tolerated. Chloroquine prophylaxis should begin 1 to 2 weeks before travel to malarious areas. It should be continued weekly during travel in malarious areas and for 4 weeks after a traveler leaves such areas. (See Table 3-8 for recommended dosages.)

Travel to Areas <u>With</u> Chloroquine-Resistant P. falciparum

For travel to areas of risk where chloroquine-resistant *P. falciparum* exists, options include the following drugs.

Mefloquine (Lariam®).—Mefloquine is usually well tolerated, but precautions should be observed (as described in "Adverse Reactions and Contraindications" on pages119 and 120 of this section). Mefloquine prophylaxis should begin 1 to 2 weeks before travel to malarious areas. It should be continued weekly during travel in malarious areas and for 4 weeks after a traveler leaves such areas. Mefloquine can be used for long-term prophylaxis. (See Table 3-8 for recommended dosages.) Note: In some foreign countries, a fixed combination of mefloquine and Fansidar® is marketed under the name Fansimef®. Fansimef® should not be confused with mefloquine, and it is not recommended for prophylaxis of malaria because of the potential for severe adverse reactions associated with prophylactic use of Fansidar® (as described in "Adverse Reactions and Contraindications," page 120).

Doxycycline.—Doxycycline is as efficacious as mefloquine for travel to most malarious areas. It can be used by travelers to areas with mefloquine-resistant strains of *P. falciparum* (the borders of Thailand with Burma [Myanmar] and Cambodia, western Cambodia, and eastern Burma). Travelers who use doxycycline should be cautioned about possible side effects (as described in "Adverse Reactions and Contraindications" on page 120 of this section). Doxycycline prophylaxis should begin 1 to 2 days before travel to malarious areas. It should be continued daily during travel in malarious areas and for 4 weeks after the traveler leaves such areas. (See Table 3-8 for recommended dosages.)

Malarone™.—Malarone™ has shown good prophylactic efficacy for prevention of *P. falciparum* malaria, including those infections acquired in areas with chloroquine-resistant strains. Recent data have demonstrated its efficacy in people without antimalarial immunity (that is, in populations whose members are similar to travelers from nonmalarious areas who travel to malarious areas, including people who formerly lived in malarious countries but who now live in nonmalarious countries), in addition to preexisting information on its good prophylactic efficacy in semi-immune people (that is, people living in malarious areas for extended periods of time). It is now one of three options (the others are mefloquine or doxycycline) for prevention of malaria when traveling to areas with chloroquine-resistant *P. falciparum* malaria. The adult dosing regimen for prophylaxis with Malarone™ is one adult tablet daily starting 1 to 2 days before travel, taken daily during travel, and continuing daily for 7 days after leaving the malarious area.

Of note, CDC no longer lists chloroquine/proguanil as an option for travel to areas with chloroquine-resistant *P. falciparum.*

Chemoprophylaxis for Infants, Children, and Adolescents

Infants, children, and adolescents of any age can contract malaria. Consequently, the indications for prophylaxis are identical to those described for adults. Chloroquine is the drug of choice for children traveling to areas without chloroquine-resistant *P. falciparum.* Data suggest that mefloquine is also well tolerated by young children (<15 kilograms [kg] [<33 pounds (lbs)]). Mefloquine is an option for use in children when travel to areas with chloroquine-resistant *P. falciparum* is unavoidable. Doxycycline is contraindicated in infants and children younger than 8 years of age. (See recommended dosages in Table 3-8.) Infants and children who cannot take mefloquine or doxycycline can be given

Malarone™ for prophylaxis. At this time, no data are available on the safety and efficacy of Malarone™ for prevention of malaria in children weighing <11 kg (<25 lbs), although studies are in progress.

Mefloquine and chloroquine phosphate are manufactured in the United States in tablet form only and have a very bitter taste. Pediatric doses should be calculated carefully according to body weight. Pharmacists can pulverize tablets and prepare gelatin capsules with calculated pediatric doses. Mixing the powder in food or drink can facilitate the administration of antimalarial drugs to infants and children. Chloroquine in suspension is widely available overseas. Physicians should calculate the dose and volume to be administered based on body weight, because the concentration of chloroquine base varies in different suspensions. Malarone™ is available in pediatric tablet form. The pediatric dosing regimen for prophylaxis (which also starts 1 to 2 days before travel, and continues during travel and for 7 days after leaving the malarious area) is contained in the Table 3-9 and is based on weight.

OVERDOSE OF ANTIMALARIAL DRUGS CAN BE FATAL.
MEDICATION SHOULD BE STORED IN CHILDPROOF CONTAINERS
OUT OF THE REACH OF INFANTS AND CHILDREN.

Chemoprophylaxis During Pregnancy

Malaria infection in pregnant women can be more severe than in nonpregnant women. Malaria can increase the risk of adverse pregnancy outcomes, including prematurity, abortion, and stillbirth. For these reasons and because no chemoprophylactic regimen is completely effective, women who are pregnant or likely to become pregnant should be advised to avoid travel to areas with malaria transmission if possible.

Chloroquine.—Women traveling to areas where drug-resistant *P. falciparum* has not been reported may take chloroquine prophylaxis. Chloroquine has not been found to have any harmful effects on the fetus when used in the recommended doses for malaria prophylaxis; therefore, pregnancy is not a contraindication for malaria prophylaxis with chloroquine or hydroxychloroquine.

Mefloquine.—A review of mefloquine use in pregnancy from clinical trials and reports of inadvertent use of mefloquine during pregnancy suggests that its use during the second and third trimesters of pregnancy is not associated with adverse fetal or pregnancy outcomes. Limited data suggest it is also safe to use during the first trimester. Consequently, mefloquine may be considered for prophylaxis in women who are pregnant or likely to become so, when exposure to chloroquine-resistant *P. falciparum* is unavoidable.

Doxycycline.—Doxycycline is contraindicated for malaria prophylaxis during pregnancy and lactation. Adverse effects of tetracyclines on the fetus include discoloration and dysplasia of the teeth

Table 3-8.—Drugs Used in the Prophylaxis of Malaria.

DRUG	USAGE	ADULT DOSE	PEDIATRIC DOSE	COMMENTS
Mefloquine (Lariam®).	In areas with chloroquine-resistant *Plasmodium falciparum.*	228 mg base (250 mg salt) orally, once/week.	15 kg or less: 4.6 mg/kg base (5 mg/kg salt) orally, once/week. 15 to 19 kg: ¼ tablet once/week. 20 to 30 kg: ½ tablet once/week. 31 to 45 kg: ¾ tablet once/week. 46 or more kg: 1 tablet once/week.	Contraindicated in people allergic to mefloquine. Not recommended for people with seizure disorders, with severe psychiatric disorders, or with cardiac conduction abnormalities.
Doxycycline	An alternative to mefloquine in areas with chloroquine-resistant *P. falciparum.*	100 mg orally, daily.	8 years of age or older: 2 mg/kg of body weight up to adult dose of 100 mg/day.	Contraindicated in children younger than 8 years of age, pregnant women, and lactating women.
Chloroquine phosphate (Aralen®)	In areas with chloroquine-sensitive *P. falciparum.*	300 mg base (500 mg salt) orally, once/week.	5 mg/kg base (8.3 mg/kg salt) orally, once/week, up to maximum adult dose of 300 mg base.	Not applicable
Hydroxy chloroquine sulfate (Plaquenil®)	An alternative to chloroquine in areas with chloroquine-sensitive *P. falciparum.*	310 mg base (400 mg salt) orally, once/week.	5 mg/kg base (6.5 mg/kg salt) orally, once/week, up to maximum adult dose of 310 mg base.	Not applicable

Atovaquone/ proguanil (Malarone™)	An alternative to mefloquine and doxycycline in areas with chloroquine-resistant *P. falciparum.*	Adult tablets contain 250 mg atovaquone and 100 mg proguanil hydrochloride. 1 adult tablet orally, daily.	Pediatric tablets contain 62.5 mg atovaquone and 25 mg proguanil hydrochloride. 11 to 20 kg: 1 tablet 21 to 30 kg: 2 tablets 31 to 40 kg: 3 tablets 40 kg or more: 1 adult tablet daily	Malarone™ should be taken with food or a milky drink. Not recommended for children <11 kg or for pregnant women.
Primaquine	Used to decrease the risk of relapses of *P. vivax* and *P. ovale.*	15 mg base (26.3 mg salt) orally, once/day for 14 days after departure from the malarious area.	0.3 mg/kg base (0.5 mg/kg salt) orally, once/day for 14 days after departure from the malarious area.	Indicated for people who have had prolonged exposure to *P. vivax* and *P. ovale* or both. Contraindicated in people with G6PD* deficiency.

Abbreviations: mg - milligram; kg - kilogram.
Kilogram = 2.2 pounds.
*Glucose-6-phosphate dehydrogenase.

Table 3-9.—Pediatric Prophylactic Doses of Malarone™.

BODY WEIGHT* (POUNDS)	BODY WEIGHT* (KILOGRAMS)	ATOVAQUONE/PROGUANIL (MALARONE™) TOTAL DAILY DOSE	DOSAGE REGIMEN
25 to 45	11 to 20	62.5 milligrams per 25 milligrams	1 pediatric tablet daily
46 to 67	21 to 30	125 milligrams per 50 milligrams	2 pediatric tablets daily
68 to 88	31 to 40	187.5 milligrams per 75 milligrams	3 pediatric tablets daily
89 or more	40 or more	250 milligrams per 100 milligrams	1 adult tablet daily

* At this time, no data are available on the safety and efficacy of Malarone™ for prevention of malaria in children weighing less than 11 kilograms (25 pounds), although studies are in progress.

and inhibition of bone growth. During pregnancy, tetracyclines are indicated only to treat life-threatening infections from multidrug-resistant *P. falciparum.*

Primaquine.—Primaquine should not be used during pregnancy because the drug can be passed transplacentally to a glucose-6-phosphate dehydrogenase (G6PD)-deficient fetus and cause hemolytic anemia in utero. Whenever radical cure or terminal prophylaxis with primaquine is indicated during pregnancy, chloroquine should be given once a week until delivery, at which time primaquine may be given.

Malarone™.—There are insufficient data regarding the use of Malarone™ during pregnancy. Therefore, Malarone™ is not currently recommended for pregnant women unless the potential benefit outweighs the potential risk to the fetus (for example, for a pregnant women who has acquired *P. falciparum* malaria in an area of multidrug-resistant strains and who cannot tolerate other treatment options).

Prophylaxis While Breast-Feeding

Data are available for some antimalarial agents on the amount of drug secreted in breast milk of lactating women. Very small amounts of chloroquine and mefloquine are secreted in the breast milk of lactating women. The amount of drug transferred is not thought to be harmful to a nursing infant. Because the quantity of antimalarials transferred in breast milk is insufficient to provide adequate protection against malaria, infants who require chemoprophylaxis should receive the recommended dosages of antimalarials listed in Table 3-8. No information is available on the amount of primaquine that enters human breast milk; the infant should be tested for G6PD deficiency before primaquine is given to a woman who is breast-feeding. Sulfonamides do enter human breast milk and should not be given to infants younger than 2 months of age. However, in most cases, the potential benefit to

the woman when Fansidar® is used for treatment of malaria would outweigh any theoretical risks to an infant.

It is not known whether atovaquone is excreted in human milk. Proguanil is excreted in human milk in small quantities. Based on experience with other antimalarial drugs, the quantity of drug transferred in breast milk is likely insufficient to provide adequate protection against malaria for the infant. Because data are not yet available on the safety and efficacy of Malarone™ in infants weighing less than 11 kg (25 lbs), it should not be given to a woman who breast feeds an infant who weighs less than 11 kg (25 lbs) unless the potential benefit to the woman outweighs the potential risk for the infant (for example, for a lactating woman who has acquired *P. falciparum* malaria in an area of multidrug-resistant strains and who cannot tolerate other treatment options).

Self-Treatment

CDC recommends the use of malaria prophylaxis for travel to malarious areas. Travelers who elect not to take prophylaxis and plan to treat themselves only if they experience symptoms or who require or choose regimens that do not have optimal efficacy (for example, use of chloroquine for travel to areas with chloroquine-resistant *P. falciparum*) should be provided with a treatment dose of one of the antimalarials recommended for presumptive self-treatment should it be needed. **Presumptive self-treatment is recommended for travelers with illness suspected to be malaria who cannot reach medical care within 24 hours**. These travelers should be advised to take presumptive self-treatment promptly if they have a febrile illness during their travel and if professional medical care is not available within 24 hours; **however, they should be advised that this self-treatment of a possible malarial infection should be only a temporary measure and that prompt medical evaluation is imperative**.

Drugs Recommended for Presumptive Self-Treatment

Fansidar®.—To date, sulfadoxine-pyrimethamine (SP) (Fansidar®) has been the drug recommended by CDC for presumptive self-treatment for travelers not allergic to sulfa drugs and remains a recommended drug for self-treatment for travelers to areas without SP resistance (see Table 3-10).

Malarone™.—Malarone™ is now another option for presumptive self-treatment for travelers not taking Malarone™ for prophylaxis. Malarone™ is the drug of choice for presumptive self-treatment for travelers to areas with SP resistance, which includes the Amazon River basin of South America, Southeast Asia, and some countries in eastern and southern Africa (specifically, Kenya, Malawi, Mozambique, South Africa, Tanzania, and Uganda). Travelers on Malarone™ prophylaxis who take presumptive self-treatment should be advised to use Fansidar® if they are traveling to an area without Fansidar® resistance. If traveling to an area with Fansidar® resistance, travelers should be advised to consult a health care provider prior to travel; CDC can provide consultation in these cases (see "Malaria Hotline," page 120, this section). (See Table 3-10 for recommended doses for medications used for presumptive self-treatment.)

Table 3-10.—Presumptive Treatment of Malaria.

DRUG	ADULT DOSE	PEDIATRIC DOSE	COMMENTS
Sulfadoxine-pyrimethamine (SP) (Fansidar®). Self-treatment drug to be used if professional medical care is not available within 24 hours. **Medical care should be sought immediately after treatment.**	3 tablets (75 mg pyrimethamine and 1,500 mg sulfadoxine), orally as a single dose.	5 to 10 kg: ½ tablet. 11 to 20 kg: 1 tablet. 21 to 30 kg: 1½ tablets. 31 to 45 kg: 2 tablets. 46 or more kg: 3 tablets.	Contraindicated in people with sulfa allergy. Resistance to SP occurs in Amazon River basin, Southeast Asia, and parts of east Africa; Malarone™ is preferred in these areas.
Atovaquone/proguanil (Malarone™).	4 tablets (each tablet contains 1,000 mg atovaquone and 400 mg proguanil) orally as a single daily dose for 3 consecutive days.	Daily dose to be taken for 3 consecutive days using adult strength tablets: 11 to 20 kg: 1 tablet 21 to 30 kg: 2 tablets 31 to 40 kg: 3 tablets 41 kg or more: 4 tablets	Not recommended for self-treatment in people on Malarone™ prophylaxis.

Abbreviations: mg - milligram; kg - kilogram.
Kilogram = 2.2 pounds.

Drugs Not Recommended for Presumptive Self-Treatment

Mefloquine.—Mefloquine should not be used for self-treatment because of the frequency of serious side effects (for example, hallucinations and seizures) that have been associated with the high doses of mefloquine used for treatment of malaria.

Halofantrine.—Halofantrine (Halfan®) is not recommended for self-treatment of malaria because of potentially serious electrocardiogram changes that have been documented following treatment doses. In many of these reports, halofantrine was administered in the presence of other antimalarial drugs (for example, mefloquine). The safety of halofantrine for self-treatment of travelers on mefloquine prophylaxis has not been established and, because halofantrine is widely available overseas, health care providers might choose to caution travelers to avoid the use of halofantrine if they are taking mefloquine.

Prevention of Relapses of *P. vivax* and *P. ovale: Primaquine*

P. vivax and *P. ovale* parasites can persist in the liver and cause relapses for as long as 4 years after routine chemoprophylaxis is discontinued. Travelers to malarious areas should be alerted to this risk and, if they develop malaria symptoms after leaving a malarious area, they should be advised to report their travel history and the possibility of malaria to a physician as soon as possible. Primaquine decreases the risk of relapses by acting against the liver stages of *P. vivax* or *P. ovale*. Primaquine is administered after the traveler has left a malaria-endemic area, usually during or following the last 2 weeks of prophylaxis.

Because most malarious areas of the world (except Haiti and the Dominican Republic) have at least one species of relapsing malaria, travelers to these areas have some risk of acquiring either *P. vivax* or *P. ovale*, although the actual risk for an individual traveler is difficult to define. Terminal prophylaxis with primaquine for prevention of relapses is generally indicated only for people who have had prolonged exposure in malaria-endemic areas (for example, missionaries and Peace Corps volunteers). Most people can tolerate the standard regimen of primaquine, with the exception of individuals deficient in G6PD. (See the following section, "Adverse Reactions and Contraindications," for a discussion of adverse reactions and Table 3-8 for recommended dosages.)

Adverse Reactions and Contraindications

Following is a discussion of the frequent or serious side effects of recommended antimalarials. In addition, physicians should review the prescribing information in standard pharmaceutical reference texts and in the manufacturers' package inserts.

Chloroquine and Hydroxychloroquine

Chloroquine and hydroxychloroquine rarely cause serious adverse reactions when taken at prophylactic doses for malaria. Minor side effects that can occur include gastrointestinal disturbance, headache, dizziness, blurred vision, and pruritus, but generally these effects do not require that the drug be discontinued. High doses of chloroquine, such as those used to treat rheumatoid arthritis, have been associated with retinopathy, but this serious side effect has not been associated with routine weekly malaria prophylaxis. Chloroquine and related compounds have been reported to exacerbate psoriasis. Chloroquine can interfere with the antibody response to human diploid cell rabies vaccine when the vaccine is administered intradermally. (See "Rabies," this chapter, pages 133 through 138.)

Mefloquine

Mefloquine is generally well tolerated when used for chemoprophylaxis. It has rarely been associated with serious adverse reactions (for example, psychoses or seizures) at prophylactic doses; these reactions are more frequent with the higher doses used in treatment. Minor side effects observed with prophylactic doses, such as gastrointestinal disturbance, insomnia, and dizziness, tend to be transient and self-limited.

Mefloquine is contraindicated for use by travelers with a known hypersensitivity to mefloquine and is not recommended for use by travelers with a history of seizures or severe psychiatric disorders. A review of available data suggests that mefloquine may be used in people concurrently on beta blockers, if they have no underlying arrhythmia. However, mefloquine is not recommended for people with cardiac conduction abnormalities.

Doxycycline

Doxycycline can cause photosensitivity, usually manifested as an exaggerated sunburn reaction. The risk of such a reaction can be minimized by avoiding prolonged, direct exposure to the sun and by using sun screens that absorb long-wave ultraviolet (UVA) radiation. In addition, doxycycline use is associated with an increased frequency of *Candida* vaginitis. Gastrointestinal side effects (nausea or vomiting) may be minimized by taking the drug with a meal. To reduce the risk of esophagitis, travelers should be advised not to take doxycycline before going to bed. Doxycycline is contraindicated in pregnancy and in infants and children younger than 8 years of age.

Malarone™

The most common adverse effects reported in people using Malarone™ for prophylaxis or treatment were abdominal pain, nausea, vomiting, and headache.

Fansidar®

Adverse reactions reported in people taking sulfonamides included nausea, vomiting, and headache. Travelers should be advised not to use Fansidar® for prophylaxis because of the risk for severe cutaneous adverse reactions. Fansidar® is contraindicated in people with a history of sulfonamide intolerance and in infants younger than 2 months of age.

Primaquine

Primaquine can cause severe hemolysis in G6PD-deficient individuals. Before primaquine is used, G6PD deficiency should be ruled out by appropriate laboratory testing.

Malaria Hotline

Detailed recommendations for the prevention of malaria are available from CDC 24 hours a day from the voice information service (1-888-232-3228) or the fax information service (1-888-232-3299), or on the Internet at http://www.cdc.gov/travel.

MEASLES (RUBEOLA)

Description

Measles is an acute, highly communicable viral disease with prodromal fever, conjunctivitis, coryza, cough, and Koplik spots on the buccal mucosa. A characteristic red blotchy rash appears around the third day of illness, beginning on the face and becoming generalized. Measles is frequently complicated by middle ear infection or diarrhea. The disease can be severe, with bronchopneumonia or brain inflammation leading to death in about 2 of every 1,000 cases.

Occurrence

Prior to widespread immunization, measles was common in childhood, with more than 90% of infants and children infected by 12 years of age. Since vaccine licensure in 1963, measles elimination efforts in the United States have resulted in record low numbers of reported measles cases. Fewer than 1,000 measles cases have been reported annually since 1993. Many of these cases were imported from outside the United States and occurred among adults; roughly half occurred in U.S. residents returning from visits to foreign countries. The risk of exposure to measles in the United States is low. Unvaccinated people can reach older ages still susceptible to measles.

Risk for Travelers

The risk of exposure to measles outside the United States could be high. Measles remains a common disease in many countries of the world, including some developed countries in Europe and Asia.

Preventive Measures

Vaccine

Measles vaccine contains live, attenuated measles virus. It is available as a single antigen preparation or combined with live, attenuated mumps or rubella vaccines, or both. Combined measles, mumps, and rubella (MMR) is recommended whenever one or more of the individual components are indicated.

Although vaccination against measles, mumps, or rubella is not a requirement for entry into any country (including the United States), people traveling or living abroad should ensure that they are immune to all three diseases. In general, travelers can be considered immune to measles if they have documentation of physician-diagnosed measles, laboratory evidence of measles immunity, or proof of receipt of two doses of live measles vaccine on or after their first birthday. Most people born before 1957 are likely to have had measles disease and generally need not be considered susceptible. However, measles or MMR vaccine may be given to these people if there is reason to believe they might be susceptible.

The first dose of MMR should be routinely administered when the infant is 12 to15 months of age. A single dose of MMR vaccine induces antibody formation to all three viruses in at least 95% of susceptibles vaccinated at 12 months of age or older. A second dose is expected to induce immunity in most vaccinees who do not respond to the first dose. The second dose should be separated from the first dose by a minimum of 28 days. See "Vaccine Recommendations for Infants and Children," page 26, for a discussion of measles immunization schedule modifications for infants who will be traveling.

MMR may be administered simultaneously (but in a different site) with any other live or inactivated vaccine. Inactivated vaccines and typhoid vaccines may be administered at any time before or after live measles-containing vaccine. However, if MMR vaccine and live yellow fever vaccine are not administered simultaneously, they should be separated by an interval of at least 28 days. (See Chapter 1, "Vaccination Information," "U.S. Public Health Service Recommendations," pages 6 through12 for more details.)

Adverse Reactions

Fever and rash are the most common adverse reactions following MMR vaccine, and are usually attributable to the measles component. About 5% of vaccinees develop fever >39.4° Celsius (>103° Fahrenheit) or a generalized rash. Fever and rash usually occur 7 to 12 days following vaccination and last for 1 or 2 days. Transient lymphadenopathy sometimes occurs following MMR and is attributable to the rubella component. Parotitis has been reported rarely following MMR and is attributable to the mumps component of the vaccine. Joint symptoms (arthralgia or arthritis, or both) are reported in up to 25% of rubella-susceptible postpubertal women who receive MMR or other rubella-containing vaccine. Joint symptoms are usually mild and transient. Allergic reactions have been reported following MMR vaccine, and range from mild (urticaria or wheal and flare at the injection site, generalized rash, and pruritus) to severe anaphylactic reactions. Severe allergic reactions are estimated to occur less than once per million doses. Clinically apparent low platelet counts have been reported at a rate of less than 1 case per 30,000 doses. Central nervous system conditions, including aseptic meningitis, encephalitis, and encephalopathy, have been reported following MMR, but are very uncommon (less than one case per million doses).

Adverse reactions occur only in susceptible vaccinees and do not appear to be age related. Reactions following the second dose of MMR (except allergic reactions) occur only among the small proportion of people who do not respond to the first dose.

Precautions and Contraindications

Allergy.—People with severe allergy (that is, hives, swelling of the mouth or throat, difficulty breathing, hypotension, and shock) to gelatin or neomycin, or who have had a severe allergic reaction to a prior dose of MMR, should not be vaccinated with MMR except with extreme caution.

In the past, people with a history of anaphylactic reactions following egg ingestion were considered to be at increased risk of serious reactions after receipt of measles- and mumps-containing vaccines, which are produced in chick embryo fibroblasts. However, recent data suggest that anaphylactic

reactions to measles- and mumps-containing vaccines are not associated with hypersensitivity to egg antigens, but to other components of the vaccines (such as gelatin). The risk for serious allergic reactions following receipt of these vaccines by egg-allergic people is extremely low and skin testing with vaccine is not predictive of allergic reaction to vaccination. MMR may be administered to egg-allergic people without prior routine skin testing or the use of special protocols.

Pregnancy.—Women known to be pregnant should not receive MMR vaccine. Pregnancy should be avoided for 1 month following receipt of monovalent measles vaccine and 3 months following MMR or other rubella-containing vaccines. Close contact with pregnant women is not a contraindication to MMR vaccination of the contact (that is, the person who will be in close proximity to the pregnant woman).

Breast-feeding is not a contraindication to MMR vaccination of either a woman or an infant. MMR vaccination has no effect on antibiotics or antimalarial drugs, and the drugs do not reduce the immunogenicity of MMR. Women taking these products should be vaccinated as usual.

Immunosuppression.—Replication of vaccine viruses can be prolonged in people who are immunosuppressed or immunodeficient for any reason (for example, who have congenital immunodeficiency, human immunodeficiency virus [HIV] infection, leukemia, lymphoma, or generalized malignancy, or who are receiving therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids). Evidence based on case reports has linked measles vaccine virus infection to subsequent death in six severely immunosuppressed people. For this reason, people who are severely immunosuppressed for any reason should not be given MMR vaccine. Healthy, susceptible close contacts of severely immunosuppressed people may be vaccinated.

In general, people receiving large daily doses of corticosteroids ($2 milligrams per kilogram [mg/kg] per day or $20 mg per day of prednisone) for 14 days or more should not receive MMR vaccine because of concern about vaccine safety. MMR and its component vaccines should be avoided for at least one month after cessation of high-dose therapy. People receiving low-dose or short-course (less than 14 days) therapy; alternate-day treatment; maintenance physiologic doses; or topical, aerosol, intra-articular, bursal, or tendon injections may be vaccinated. Although people receiving high doses of systemic corticosteroids daily or on alternate days during an interval of less than 14 days generally can receive MMR or its component vaccines immediately after cessation of treatment, some experts prefer waiting until 2 weeks after completion of therapy.

People receiving cancer chemotherapy or radiation who have not received these treatments for at least 3 months may receive MMR or its component vaccines.

Measles disease can be severe in people with HIV infection. Available data indicate that vaccination with MMR has not been associated with severe or unusual adverse events in HIV-infected people without evidence of severe immunosuppression, although antibody responses have been variable. MMR vaccine is recommended for all asymptomatic HIV-infected people and should be considered for symptomatic people who are not severely immunosuppressed. Asymptomatic HIV-infected infants, children, and adolescents do not need to be evaluated and tested for HIV infection before

MMR or other measles-containing vaccines are administered. A theoretical risk of an increase (probably transient) in HIV viral loading following MMR vaccination exists because such an effect has been observed with other vaccines. The clinical significance of such as increase is not known.

MMR and other measles-containing vaccines are not recommended for HIV-infected people with evidence of severe immunosuppression (for example, people with a very low CD4+ T-lymphocyte count), primarily because of the report of a case of measles pneumonitis in a measles vaccinee who had an advanced case of acquired immunodeficiency syndrome (AIDS). Refer to the Advisory Committee on Immunization Practices (ACIP) statement on MMR for additional details on vaccination of people with symptomatic HIV infection.

Acute Illness.—Vaccination of travelers with moderate or severe acute illness should be postponed until their condition has improved. Minor illnesses, such as upper respiratory infections with or without low-grade fever, do not preclude vaccination.

Immune Globulin (IG) or Other Antibody-Containing Blood Products.—MMR or its component vaccines should be administered at least 14 days before the administration of antibody-containing blood products, such as immune globulin (IG). Because passively acquired antibodies might interfere with the response to the vaccine, MMR should be delayed following administration of blood products. The length of delay varies from 3 to 11 months, depending on the type of blood product received. (See Chapter 1, "Vaccination Information," "U.S. Public Health Service Recommendations," pages 6 through 12 for more details.)

Tuberculosis.—Tuberculosis can be exacerbated by measles disease. There is no evidence, however, that live measles virus vaccine has such an effect. Purified protein derivative (PPD) tuberculin testing is not a prerequisite for vaccination with MMR or other measles-containing vaccine. PPD testing has no effect on the response to MMR vaccination. However, measles vaccine (and possibly mumps, rubella, and varicella vaccines) can suppress the response to PPD in a person infected with *Mycobacterium tuberculosis.* To minimize the risk of a false-negative interpretation, PPD testing should be delayed for 4 to 6 weeks after MMR vaccination. If PPD testing is needed, it should be done prior to MMR vaccination. It is also acceptable to apply the PPD and administer MMR simultaneously, because the mild immunosuppressive effect of the vaccine will not occur for several days after vaccination.

MENINGOCOCCAL DISEASE

Description

Meningococcal disease is an acute bacterial disease characterized by sudden onset with fever; intense headache; nausea and often vomiting; stiff neck; and, frequently, a petechial rash with pink macules. Formerly, case-fatality rates exceeded 50% but, with early diagnosis, modern therapy, and

supportive measures, the case-fatality rate is now from 5% to 15%. Up to 10% of populations in countries with endemic disease might be asymptomatic carriers.

Occurrence

In sub-Saharan Africa, epidemics of serogroup A or C meningococcal disease occur frequently during the dry season (December through June), particularly in the savannah areas extending from Mali eastward to Ethiopia, known as the "meningitis belt" (see Map 3-5).

Risk for Travelers

Meningococcal disease in Americans traveling in sub-Saharan Africa is rare. However, because of the lack of established surveillance and timely reporting from many of these countries, travelers to the meningitis belt during the dry season should be advised to receive meningococcal vaccine, especially if prolonged contact with the local population is likely.

Preventive Measures

Vaccine

Vaccination against meningococcal disease is not a requirement for entry into any country, except to Mecca, Saudi Arabia, for travelers during the annual Hajj. Vaccination is indicated for travelers to countries recognized as having epidemic meningococcal disease caused by a vaccine-preventable serogroup (that is, A, C, Y, and W-135). Advisories for travelers to other countries will be issued when epidemics of meningococcal disease caused by vaccine-preventable serogroups are recognized. (See the Centers for Disease Control and Prevention [CDC] Travelers' Health website http://www.cdc.gov/travel.)

Serogroup A is the most common cause of epidemics outside the United States, but serogroup C and serogroup B can also cause epidemic disease. One formulation of meningococcal polysaccharide vaccine is currently available in the United States: quadrivalent A, C, Y, and W-135 vaccine (Table 3-11). The vaccine is available in single- and multiple-dose vials, and is distributed in the United States by Aventis Pasteur. No vaccine is yet available to offer protection against serogroup B. Meningococcal vaccines are chemically defined antigens consisting of purified bacterial capsular polysaccharides, each inducing serogroup-specific immunity. Serogroup A vaccine has not been shown to be effective in infants younger than 3 months of age and can be less than fully effective in infants 3 through 11 months of age. Serogroup C vaccine has not been shown to be effective in infants younger than 2 years of age. The group Y and W-135 polysaccharides have been shown to be safe and immunogenic in adults; the response of infants to these polysaccharides is unknown.

Areas with Frequent Epidemics of Meningococcal Meningitis

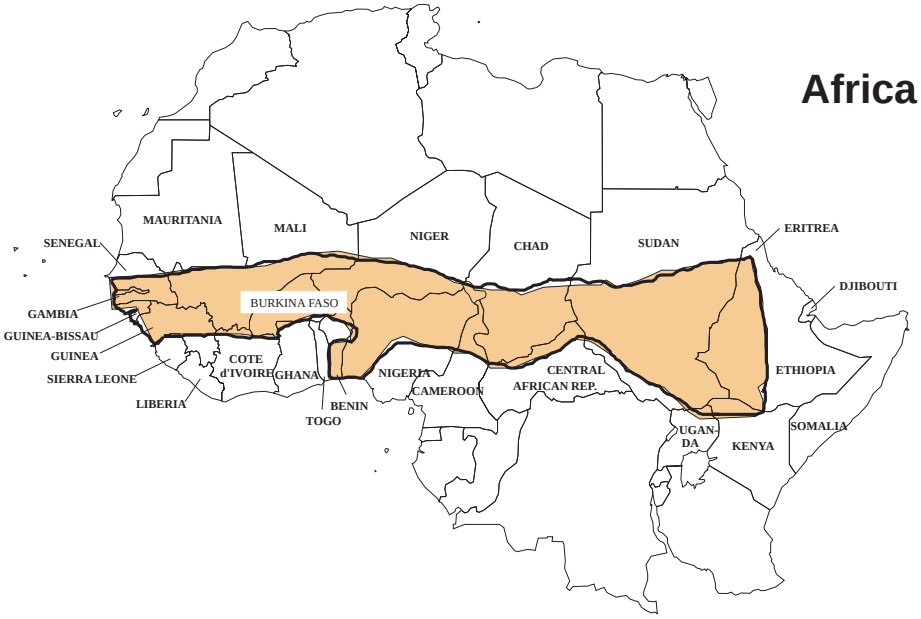


Table 3-11.—Meningococcal Vaccine.

TYPE OF VACCINE	DOSE	COMMENTS
Quadrivalent A,C,Y,W–135	0.5 milliliter	Duration of immunity is unknown, but appears to be at least 3 years in those 4 years of age or older. Revaccination after 2 to 3 years should be considered for children first vaccinated before 4 years of age who continue to be at high risk.

For subcutaneous injection.

Adverse Reactions

Adverse reactions to meningococcal vaccine are infrequent and mild, consisting principally of localized erythema that lasts 1 to 2 days. Up to 2% of infants develop fever transiently after vaccination.

Precautions and Contraindications

Studies of vaccination during pregnancy have not documented adverse effects among either women or neonates (1 month of age or younger). Based on data from studies involving the use of meningococcal vaccines and other polysaccharide vaccines administered during pregnancy, altering meningococcal vaccination recommendations during pregnancy is unnecessary.

MUMPS

Description

Mumps is an acute viral disease characterized by fever, swelling, and tenderness of one or more salivary glands, usually the parotid and sometimes the sublingual or submaxillary glands.

Occurrence

Prior to vaccine licensure in 1967, 100,000 to 200,000 mumps cases are estimated to have occurred in the United States each year. Incidence declined to approximately 5,000 cases per year during the period from 1980 to 1990. Since 1995, fewer than1,000 cases have been reported annually. The decline since 1995 is believed to be a result of the widespread use of a second dose of measles,

mumps, and rubella (MMR) vaccine. Mumps primarily affects school-aged children. Since 1982, 50% to 80% of reported cases have occurred among those 5 through 19 years of age.

Risk for Travelers

The risk for exposure to mumps outside the United States can be high. Few countries use mumps vaccine, so mumps remains a common disease in many countries of the world.

Preventive Measures

Vaccine

Mumps vaccine contains live, attenuated mumps virus. It is available as a single antigen preparation, or combined with live, attenuated measles or rubella vaccines, or both. Combined MMR is recommended whenever one or more of the individual components are indicated.

Although vaccination against measles, mumps, and rubella is not a requirement for entry into any country (including the United States), people traveling or living abroad should be advised to ensure that they are immune to all three diseases. Immunity to mumps is of particular importance for children approaching puberty, and for adolescents and adults, particularly males, who have not had mumps. People can be considered immune to mumps if they have documentation of receipt of one or more doses of a mumps-containing vaccine on or after their first birthday or physician-diagnosed mumps, or laboratory evidence of mumps immunity. Most adults born before 1957 are likely to have been infected naturally and generally can be considered immune, even if they did not have clinically recognizable disease. However, mumps or MMR vaccine may be given to older people if there is reason to believe they might be susceptible.

The first dose of MMR should be routinely administered when an infant is 12 to 15 months of age. A single dose of MMR vaccine induces antibody formation to all three viruses in at least 95% of susceptibles vaccinated at 12 months of age or older. A second dose is expected to induce immunity in most vaccinees who do not respond to the first dose. The second dose should be separated from the first dose by a minimum of 28 days. (See Chapter 1, “Vaccine Information,” “Vaccine Recommendations for Infants and Children,” pages 12 through 21, for a discussion of mumps immunization schedule modifications for infants who will be traveling.)

Adverse Reactions

Refer to the “Measles” section of this chapter (page 122) for information on adverse reactions following MMR vaccine.

Precautions and Contraindications

Refer to the “Measles” section of this chapter (pages 122 through 124) for information on precautions and contraindications for MMR vaccine.

ONCHOCERCIASIS (RIVER BLINDNESS)

Description

Onchocerciasis is caused by the prelarval (microfilaria) and adult stages of the nematode *Onchocerca volvulus* and can result in dermatitis; subcutaneous nodules; lymphadenitis; and visual impairment, including blindness. The disease is transmitted by the bite of female *Simulium* flies (black flies) that bite by day and are found near rapidly flowing rivers and streams.

Occurrence

Onchocerciasis is endemic in more than 25 nations located in a broad band across the central part of Africa. Small endemic foci are also present in the Arabian peninsula (Yemen) and in South and Central America (Brazil, Colombia, Ecuador, Guatemala, southern Mexico, and Venezuela).

Risk for Travelers

Those traveling for less than 3 months in onchocerciasis-endemic regions appear to be at low risk for acquiring this condition. However, temporary residents and others who visit endemic regions for longer than 3 months and live or work near black fly habitats are at greater risk for infection. Infections tend to occur in expatriate groups such as missionaries, field scientists, and Peace Corps volunteers.

Preventive Measures

No vaccine and no effective chemoprophylaxis are available. Protective measures include avoidance of black fly habitats and the use of personal protection measures against biting insects such as those outlined in Chapter 4, "Health Hints for the International Traveler," "Protection Against Mosquitoes and Other Arthropod Vectors," pages 163 through 165.

Treatment

Ivermectin is the drug of choice for onchocerciasis. Repeat (that is, annual) doses are required because the drug kills the microfilaria, but not the adult worm. Travelers should be advised to consult with a specialist in infectious diseases or tropical medicine.

PLAGUE

Description

Plague is a zoonosis involving rodents and their fleas. The causative agent of plague is a bacterium, *Yersinia pestis*. Humans are incidental hosts and are usually infected by the bite of rodent fleas. Plague can also be acquired by direct contact with infectious materials or by inhalation of infective respiratory droplets. Initial signs and symptoms of plague can be nonspecific, with fever, chills, malaise, myalgia, nausea, prostration, sore throat, and headache. Bubonic plague, the most common form, usually presents with painful, swollen lymph nodes (buboes) that develop in the afferent lymphatic chain draining the site of the flea bite.

Plague continues to be enzootic in wild rodent populations over large rural areas of the Americas, Africa, and Asia, with occasional outbreaks among commensal rodents in villages and small towns. Wild rodent plague poses a real, though limited, risk to people. When infection spreads to rats in urban or populated areas, people are at markedly increased risk of exposure. In the past several decades, however, urban outbreaks have been rare and limited in size.

Occurrence

Wild rodent plague exists in the western third of the United States, in widely scattered areas of South America; in north-central, eastern, and southern Africa; in Madagascar; in Iranian Kurdistan; along the frontier between Yemen and Saudi Arabia; in central and southeast Asia (Burma [Myanmar], China, India, Indonesia, Kazakhstan, Mongolia, and Vietnam); and in portions of Russia. In recent years, human plague has been reported in Africa from Angola, Botswana, Democratic Republic of the Congo (Zaire), Kenya, Libya, Madagascar, Malawi, Mozambique, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe; in Asia from Burma [Myanmar], China, India, Kazakhstan, Laos, Mongolia, and Vietnam; and in the Americas from Bolivia, Brazil, Ecuador, Peru, and the United States.

Risk for Travelers

Risk to travelers in any of these areas is small.

Preventive Measures

Vaccine

Plague vaccine is no longer commercially available. Vaccination against plague is not required by any country as a condition for entry. In the past, vaccine was recommended only for people who were at a particularly high risk of exposure because they worked with plague routinely in the laboratory or because of field exposures to rodents and their fleas in epizootic areas. In most of the countries of Africa, Asia, and the Americas where plague is reported, the risk of infection exists primarily in

rural mountainous or upland areas. People who travel to plague-infected areas should follow the preventive measures described in the following section.

Other

Travelers considered to be at high risk for plague because of unavoidable exposures in active epizootic or epidemic areas should be advised to consider antibiotic chemoprophylaxis with tetracycline or doxycycline during periods of exposure. Trimethoprim-sulfamethoxazole is an acceptable substitute for use in infants and in children younger than 8 years of age. Personal protective measures should also be recommended, including the use of insect repellents containing N,N-diethylmetatoluamide (DEET) on skin and clothing. Clothing also can be treated with insecticidal sprays containing permethrin. Travelers should be advised to avoid sick or dead animals or rodent nests and burrows. Whenever possible, travelers should also avoid visiting areas that have experienced recent plague epidemics or epizootics. Travelers are unlikely to be at high risk for plague while staying in modern accommodations.

POLIOMYELITIS

Description

Poliomyelitis is an acute infection that involves the gastrointestinal tract and, occasionally, the central nervous system. It is acquired by fecal-oral transmission. Clinical manifestations of poliovirus infection range from asymptomatic (the majority of infections) to symptomatic, including acute flaccid paralysis of a single limb to quadriplegia; respiratory failure; and, rarely, death.

Occurrence

In the prevaccine era, infection with poliovirus was common, with epidemics occurring in the summer and fall in temperate areas. The incidence of poliomyelitis fell rapidly after the licensure of inactivated polio vaccine in 1955 and oral polio vaccine in the 1960s. The last cases of indigenously acquired polio in the United States occurred in 1979. Although a polio eradication program led to elimination of polio in the Western Hemisphere, where the last case associated with wild poliovirus was detected in 1991, an outbreak of vaccine-derived poliovirus type 1 occurred in the Dominican Republic and Haiti in July 2000. In spite of this recent outbreak in the Western Hemisphere, the global polio eradication initiative has reduced the number of reported polio cases worldwide by >90% since the mid-1980s, and worldwide eradication of the disease appears feasible in the near future.

Risk for Travelers

Travelers to countries where polio is epidemic or still endemic should be fully immunized. Because of polio eradication efforts, the number of countries where travelers are at risk for polio has decreased dramatically. Concurrent with the decline in polio incidence, the number of polio-endemic countries

decreased from more than 120 in 1988 to approximately 50 in 1998. Approximately 75% of the world's population resides in areas now considered free of wild poliovirus circulation, including the Western Hemisphere, the Western Pacific Region (which encompasses China), and the European region. Most of the world's remaining poliovirus transmission is in two large endemic areas in south Asia and sub-Saharan Africa. Accelerated polio eradication strategies are being used in seven reservoir countries—Bangladesh, Democratic Republic of the Congo, Ethiopia, India, Nepal, Nigeria, and Pakistan—as well as in Afghanistan, Angola, Liberia, Sierra Leone, Somalia, Sudan, and Tajikistan.

Preventive Measures

Vaccine

A person is considered to be fully immunized if he or she has received a primary series of at least three doses of inactivated poliovirus vaccine (IPV), live oral poliovirus (OPV), or any combination of IPV and OPV. To eliminate the risk for vaccine-associated paralytic poliomyelitis, OPV was no longer recommended for routine immunization in the United States as of January 1, 2000. Manufacture of the only OPV licensed for use in the United States has ceased, and OPV is no longer available in this country. OPV remains the vaccine of choice, however, for global polio eradication activities.

Infants and Children

Because OPV is no longer recommended for routine immunization in the United States, all infants and children should receive four doses of IPV at 2, 4, and 6 through 18 months of age, and 4 through 6 years of age. If accelerated protection is needed, the minium interval between doses is 4 weeks, although the preferred interval between the second and third doses is 2 months. Infants and children who have initiated the poliovirus vaccination series with one or more doses of OPV should receive IPV to complete the series.

Adults

Adults who are traveling to polio-endemic areas and are unimmunized or whose vaccination status is unknown should receive IPV. Two doses of IPV should be administered at intervals of 4 to 8 weeks; a third dose should be administered 6 to 12 months after the second. If three doses of IPV cannot be administered within the recommended intervals before protection is needed, the following alternatives are recommended:

- If more than 8 weeks is available before protection is needed, three doses of IPV should be administered at least 4 weeks apart.
- If less than 8 weeks, but more than 4 weeks, is available before protection is needed, two doses of IPV should be administered at least 4 weeks apart.
- If less than 4 weeks is available before protection is needed, a single dose of IPV is recommended.

The remaining doses of vaccine should be administered later, at the recommended intervals, if the person remains at increased risk for poliovirus exposure. Adults who are traveling to polio-endemic areas and have received a primary series with either IPV or OPV can receive another dose of IPV. Available data do not indicate the need for more than a single lifetime booster dose with IPV for adults.

Adverse Reactions

Allergy.—Minor local reactions (pain and redness) can occur following IPV. No serious adverse reactions to IPV have been documented.

IPV should not be administered to people who have experienced a severe allergic (anaphylactic) reaction after a previous dose of IPV or to streptomycin, polymixin B, or neomycin. Because IPV contains trace amounts of streptomycin, polymixin B, and neomycin, hypersensitivity reactions can occur among people sensitive to these antibiotics.

Pregnancy.—Although no adverse events of IPV have been documented among pregnant women or their fetuses, vaccination of pregnant women should be avoided on theoretical grounds. However, if a pregnant woman is unimmunized and requires immediate protection against polio, IPV can be administered as recommended in the adult schedule. Breast-feeding does not interfere with successful immunization against polio.

Precautions and Contraindications

A dose of IPV may be administered to an infant or a child with diarrhea. Minor upper respiratory illnesses with or without fever; mild to moderate local reactions to a previous dose of IPV; current antimicrobial therapy; and the convalescent phase of acute illness are not contraindications for vaccination.

Immunosuppression.—IPV is the only polio vaccine recommended for use in immunodeficient travelers and their household contacts. Many immunodeficient people are immune to polioviruses as a result of previous vaccination or exposure to the wild virus when they were immunocompetent. Administration of IPV to immunodeficient travelers is safe. Although a protective immune response cannot be ensured, IPV might confer some protection.

RABIES

Description

Rabies is an acute, fatal encephalomyelitis caused by neurotropic viruses in the family Rhabdoviridae, genus Lyssavirus, almost always transmitted by an animal bite that innoculates the virus into wounds. Very rarely rabies has been transmitted by nonbite exposures that introduce the virus into open wounds or mucous membranes. The disease progresses from a nonspecific prodromal phase to paresis

or paralysis; spasms of swallowing muscles can be stimulated by the sight, sound, or perception of water (hydrophobia); delirium and convulsions can develop, followed by coma and death. All mammals are believed to be susceptible, but reservoirs consist of carnivores and bats. Although dogs are the main reservoir in developing countries, the epidemiology of the disease differs sufficiently from one region or country to another to warrant the medical evaluation of all mammal bites.

Occurrence

Rabies is found on all continents, except Antarctica. In certain areas of the world, canine rabies remains highly endemic, including (but not limited to) parts of Brazil, Bolivia, Colombia, Ecuador, El Salvador, Guatemala, India, Mexico, Nepal, Peru, the Philippines, Sri Lanka, Thailand, and Vietnam. The disease is also found in dogs in most of the other countries of Africa, Asia, and Central and South America, except as may be noted in Table 3-12.

Table 3-12 lists countries that have reported no cases of rabies during the most recent 2-year period for which information is available (formerly referred to as "rabies-free countries"). Additional information can be obtained from the local health authorities of the country, the embassy, or the local consulate's office in the United States.

Risk for Travelers

Travelers to rabies-endemic countries should be warned about the risk of acquiring rabies, although rabies vaccination is not a requirement for entry into any country. Travelers with extensive unprotected outdoor, evening, and nighttime exposure in rural areas, such as might be experienced while bicycling, camping, or engaging in certain occupational activities, might be at high risk even if their trip is brief.

Preventive Measures

Vaccine

Preexposure vaccination with human diploid cell rabies vaccine (HDCV), purified chick embryo cell (PCEC) vaccine, or rabies vaccine adsorbed (RVA) may be recommended for international travelers based on the local incidence of rabies in the country to be visited, the availability of appropriate antirabies biologicals, and the intended activity and duration of stay of the traveler. Preexposure vaccination may be recommended for veterinarians, animal handlers, field biologists, spelunkers, missionaries, and certain laboratory workers. Table 3-13 provides criteria for preexposure vaccination. Preexposure vaccination does not eliminate the need for additional medical attention after a rabies exposure, but simplifies postexposure prophylaxis in populations at risk by eliminating the need for rabies immune globulin (RIG) and by decreasing the number of doses of vaccine required. Preexposure vaccination is of particular importance for travelers at risk of exposure to

Table 3-12.—Countries and Political Units Reporting No Cases of Rabies During 1997 and 1998.*

REGION		COUNTRIES
Africa		Cape Verde, Libya, Mauritius, Réunion, and Seychelles
Americas	North:	Bermuda; Saint Pierre and Miquelon
	Carribbean:	Antigua and Barbuda, Aruba, Bahamas, Barbados, Cayman Islands, Guadeloupe, Jamaica, Martinique, Montserrat Netherlands Antilles (Bonaire, Curaçao, Saba, Sint Maarten, and Saint Eustatius), Saint Kitts (Saint Christopher) and Nevis, Saint Lucia, Saint Martin, Saint Vincent and Grenadines, and Virgin Islands (U.K. and U.S.)
	South:	Uruguay
Asia		Armenia, Bahrain, Brunei, Cyprus, Hong Kong, Japan, Kuwait, Malaysia (Sabah and Sarawak), Maldives, Qatar, Singapore, Taiwan, and United Arab Emirates
Europe		Albania, Andorra, Faroe Islands, Finland, Gibraltar, Greece, Iceland, Ireland, Isle of Man, Italy, Jersey, Malta, Monaco, Norway (mainland), Portugal, Spain*(except Ceuta/Melilla), Sweden, Switzerland, and United Kingdom
Oceania†		Australia*, Cook Islands, Fiji, French Polynesia, Guam, Kiribati, New Caledonia, New Zealand, Palau, Papua New Guinea, Samoa, and Vanuatu

*Bat rabies might exist in some areas that are free of terrestrial rabies.
† Most of Pacific Oceania is reportedly "rabies-free."

rabies in countries where the locally available rabies vaccines might carry a high risk of adverse reactions. Preexposure vaccination can also provide protection when there is an unapparent or unrecognized exposure to rabies and when postexposure prophylaxis might be delayed.

Purified equine rabies immune globulin (ERIG) has been used effectively in developing countries where human rabies immune globulin (RIG) might not have been available. If necessary, such heterologous product is preferable to no RIG administration in human rabies postexposure prophylaxis. The incidence of adverse reactions after the use of these products has been low (0.8% to 6.0%), and most of those that occurred were minor. However, such products are neither evaluated by U.S. standards nor regulated by the U.S. Food and Drug Administration, and their use cannot be unequivocally recommended at this time. In addition, unpurified antirabies serum of equine origin might still be used in some countries where neither human RIG nor ERIG are available. The use of this antirabies serum is associated with higher rates of serious adverse reactions, including anaphylaxis.

Table 3-13.—Criteria for Preexposure Immunization.

RISK CATEGORY	NATURE OF RISK	TYPICAL POPULATIONS	PREEXPOSURE REGIMEN
Continuous	Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, nonbite, or aerosol exposure.	Rabies research laboratory workers;* rabies biologics production workers.	Primary course: Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level.†
Frequent	Exposure usually episodic with source recognized, but exposure might also be unrecognized. Bite, nonbite, or aerosol exposure possible.	Rabies diagnostic laboratory workers,* spelunkers, veterinarians and staff, and animal control and wildlife workers in rabies-epizootic areas.	Primary course: Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level.†
Infrequent (greater than general population)	Exposure nearly always episodic with source recognized. Bite or nonbite exposure.	Veterinarians, animal control and wildlife workers in areas with low rabies rates; veterinary students; and travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care, including biologics, is limited.	Primary course: No serologic testing or booster vaccination.
Rare (general population)	Exposure always episodic, with source recognized. Bite or nonbite exposure.	U.S. population at large, including individuals in rabies-epizootic areas.	No preexposure immunization necessary.

*Judgement of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor (see U.S. Department of Health and Human Service's Biosafety in Microbiological and Biomedical Laboratories, 1984).

†Preexposure booster immunization consists of one dose of human diploid cell [rabies] vaccine (HDCV), purified chick embryo cell (PCEC) vaccine, or rabies vaccine adsorbed (RVA), 1.0 milliliter (mL) dose, intramuscular (IM) (deltoid area), or HDCV, 0.1 mL intradermal (ID) (deltoid). Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if titer falls below this level.

Table 3-14.—Preexposure Immunization.*

VACCINE	DOSE	NUMBER OF DOSES	SCHEDULE (DAYS)	ROUTE
HDCV	0.1 mL 1.0 mL	3 3	0, 7, 21 or 28 0, 7, 21 or 28	Intradermal† Intramuscular
PCEC	1.0 mL	3	0, 7, 21 or 28	Intramuscular
RVA	1.0 mL	3	0, 7, 21 or 28	Intramuscular

Abbreviations: HDCV - human diploid cell vaccine; PCEC - purified chick embryo cell; RVA - rabies vaccine adsorbed; mL - milliter.
*Preexposure immunization of immunosuppressed travelers is not recommended.
†If the traveler will be taking chloroquine or mefloquine for malaria chemoprophylaxis, the three-dose series must be completed before antimalarials are begun. If this is not possible, the intramuscular dose and route should be used. Administration of routine booster doses of vaccine depends on exposure risk category as noted in Table 3-13.

Travelers should be advised that any animal bite or scratch should receive prompt local treatment by thorough cleansing of the wound with copious amounts of soap and water; this local treatment will significantly reduce the risk of rabies. Travelers who might have been exposed to rabies should be advised to always contact local health authorities immediately for advice about postexposure prophylaxis and should also contact their personal physician or state health department as soon as possible thereafter.

Tables 3-14 and 3-15 provide information on preexposure and postexposure prophylaxis. Routine serologic testing is not necessary for travelers who receive the recommended preeexposure or postexposure regimen with HDCV, PCEC, or RVA vaccines. Exposed travelers previously vaccinated with noncell culture vaccines should receive the complete postexposure regimen unless they have developed a laboratory-confirmed antibody response to the primary vaccination. Serologic testing is still recommended for travelers whose immune response might be diminished by drug therapy or by diseases. Rabies preexposure prophylaxis might not be indicated for travelers to the countries in Table 3-12, and postexposure prophylaxis is rarely necessary after exposures to terrestrial animals in these countries.

Chloroquine phosphate (and possibly other structurally related antimalarials such as mefloquine, administered for malaria chemoprophylaxis) might interfere with the antibody response to HDCV when administered by the intradermal (ID) route. The intramuscular (IM) route of preexposure prophylaxis, however, provides a sufficient margin of safety in this setting. HDCV should not be administered by the ID route when chloroquine, mefloquine, or other drugs that might interfere with the immune response are being used. For international travelers, the ID route should be initiated early, to allow the three-dose series to be completed before antimalarials are begun; otherwise, the IM route should be used. PCEC and RVA should never be administered ID.

Table 3-15.—Postexposure Immunization.*

IMMUNIZATION STATUS	VACCINE/ PRODUCT	DOSE	NUMBER OF DOSES	SCHEDULE (DAYS)	ROUTE
Not previously immunized	RIG	20 I.U./kg body weight	1	0	Infiltrated at bite site (if possible); remainder intramuscular.
	HDCV PCEC RVA	1.0 mL	0	0, 3, 7, 14, 28	Intramuscular
Previously immunized†	HDCV PCEC RVA§	1.0 mL	2	0,3	Intramuscular

Abbreviations: RIG - rabies immune globulin; HDCV - human diploid cell [rabies] vaccine; PCEC - purified chick embryo cell; RVA - rabies vaccine adsorbed; I.U. - international unit; kg - kilogram; mL - milliliter.
*All post-exposure treatment should begin with immediate thorough cleansing of all wounds with soap and water.
†Pre-exposure immunization with HDCV, PCEC, or RVA; prior post-exposure prophylaxis with HDCV, PCEC, or RVA; or people previously immunized with any other type of rabies vaccine **and** a documented history of positive antibody response to the prior vaccination.
§RIG should not be administered.

Adverse Reactions

Travelers should be advised that they can experience local reactions such as pain, erythema, and swelling or itching at the injection site, or mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness. Approximately 6% of people receiving booster vaccinations with HDCV can experience an immune complex-like reaction characterized by urticaria, pruritus, and malaise. Once initiated, rabies postexposure prophylaxis should not be interrupted or discontinued because of local or mild systemic reactions to rabies vaccine.

Precautions and Contraindications

Pregnancy.—Pregnancy is not a contraindication to postexposure prophylaxis.

Age.—In infants and children, the dose of HDCV, PCEC, or RVA for preexposure or postexposure prophylaxis is the same as that recommended for adults. The dose of RIG for postexposure prophylaxis is based on body weight (Table 3-15).

RIFT VALLEY FEVER

Description

Rift Valley fever (RVF) is a viral disease that affects primarily livestock and people. It is transmitted by several means, including the bites of mosquitoes and other biting insects, and percutaneous inoculation or inhalation of aerosols from contaminated blood or fluids of infected animals.

Occurrence

Occasionally, outbreaks occur involving large numbers of human cases, for example, in the Nile delta, Egypt (1978 and 1993), and the lower Senegal River basin of Mauritania (1987). A large epidemic also occurred in Kenya and Tanzania in 1997 and 1998. A recent outbreak (2000) of RVF occurred in southwestern Saudi Arabia and Yemen with a strain of RVF closely related to that of the 1997–1998 strain. This represented the first spread of the virus outside Africa, demonstrating its potential for spread to unaffected regions elsewhere in the tropics.

Risk for Travelers

The risk of RVF infection to people who travel to endemic areas is generally low. Risk factors for acquisition of RVF include exposure to the blood or tissues of sick animals, or exposure to infected mosquitoes.

Preventive Measures

No vaccine is available for human use. An inactivated and a live, attenuated vaccine (MP-12) are currently under evaluation for use in humans, but have not yet been approved by the U.S. Food and Drug Administration. Travelers should be advised that they can reduce their risk of exposure by avoiding contact with livestock and minimizing their exposure to arthropod bites by using permethrin-impregnated bednets and insect repellents.

RUBELLA

Description

Rubella is an acute viral disease that can affect susceptible people of any age. Although generally mild in infants and children, rubella can be associated with significant morbidity in adults and is associated with a high rate of fetal wastage or anomalies if contracted in the early months of pregnancy.

Occurrence

The largest annual total number of cases of rubella in the United States occurred in 1969, when 57,686 cases were reported. Following vaccine licensure in 1969, rubella incidence fell rapidly. Since 1992, fewer that 500 cases have been reported each year. However, the proportion of reported rubella cases among adults 20 years of age or older has risen steadily from 29% in 1991 to 74% in 1999. Since 1992, an average of six cases of congenital rubella syndrome (CRS) have been reported annually. Most people 20 through 30 years of age with rubella, as well as the mothers of all infants with CRS, were born outside the United States in areas where rubella vaccine is not routinely given.

Risk for Travelers

Rubella occurs worldwide, and the risk of exposure to rubella outside the United States can be high. Few countries routinely use rubella vaccine, so rubella remains a common disease in many countries in the world.

Preventive Measures

Vaccine

Rubella vaccine contains live, attenuated rubella virus. It is available as a single antigen preparation or combined with live, attenuated measles or mumps vaccines, or both. Combined measles, mumps, and rubella (MMR) vaccine is recommended whenever one or more of the individual components is indicated.

Although vaccination against measles, mumps, or rubella is not a requirement for entry into any country (including the United States), people traveling or living abroad should ensure that they are immune to all three diseases. Immunity to rubella is particularly important for women of childbearing age. People can be considered immune to rubella if they have documentation of receipt of one or more doses of a rubella-containing vaccine on or after their first birthday, or laboratory evidence of rubella immunity. Birth before 1957 provides only presumptive evidence of rubella immunity and does not guarantee that a person is immune. Rubella can occur in susceptible people born before 1957, and CRS can occur in the offspring of women infected with rubella during pregnancy. The Advisory Committee on Immunization Practices (ACIP) recommends that birth before 1957 not be accepted as evidence of rubella immunity for women who might become pregnant. A clinical diagnosis of rubella is unreliable and should not be considered in assessing immune status. Because many rash illnesses can mimic rubella infection and many rubella infections are unrecognized, the only reliable evidence of previous rubella infection is the presence of serum rubella IgG or documentation of prior vaccination.

The first dose of MMR should be routinely administered when an infant is 12 to 15 months of age. A single dose of MMR vaccine induces antibody formation to all three viruses in at least 95% of susceptibles vaccinated at 12 months of age or older. The second dose should be separated from the

first dose by a minimum of 28 days. (See Chapter 1, "Vaccination Information, "Vaccine Recommendations for Infants and Children," pages 12 through 21 for a discussion of the rubella immunization schedule modifications for infants who will be traveling.)

Adverse Reactions

Refer to the "Measles" section of this chapter (page 122) for information on adverse reactions following MMR vaccine.

Precautions and Contraindications

Refer to the "Measles" section of this chapter (pages 122 through 124) for information on precautions and contraindications for MMR vaccine.

SCHISTOSOMIASIS

Description

Schistosomiasis is caused by flukes, whose complex life cycles involve specific fresh-water snail species as intermediate hosts. Infected snails release large numbers of minute, free-swimming larvae (cercariae) that are capable of penetrating the unbroken skin of the human host. Even brief exposure to contaminated water can result in infection, for example, by wading or swimming in or bathing with contaminated fresh water. Human schistosomiasis cannot be acquired by wading or swimming in salt water (oceans or seas).

Clinical manifestations of acute infection can occur within 2 to 3 weeks of exposure to cercariae-infested water, but most acute infections are asymptomatic. The most common acute symptoms are fever, lack of appetite, weight loss, abdominal pain, weakness, headaches, joint and muscle pain, diarrhea, nausea, and cough. Rarely, the central nervous system can be involved, producing seizures or transverse myelitis as a result of mass lesions of the brain or spinal cord. Chronic infections can cause disease in the lungs, liver, intestines, or bladder, or a combination of these. Many people who develop chronic infections can recall no symptoms of acute infection. Diagnosis of infection is usually confirmed by serologic studies or by finding schistosome eggs on microscopic examination of stool or urine. Schistosome eggs can be found as soon as 6 to 8 weeks after exposure, but are not invariably present.

Occurrence

This infection is estimated to occur worldwide among some 200 million people. Schistosomiasis is most prevalent in Brazil; Egypt and most of sub-Saharan Africa; and southern China, the Philippines, and Southeast Asia.

Risk for Travelers

Exposure to schistosomiasis is a health hazard for U.S. citizens who travel to endemic areas of the Caribbean, South America, Africa, and Asia. Outbreaks of schistosomiasis have occurred among adventure travelers participating in river trips in Africa, as well as among resident expatriates such as Peace Corps volunteers in high-risk areas. Those at greatest risk are travelers who engage in wading or swimming in or bathing with fresh water in areas where poor sanitation and appropriate snail hosts are present.

Preventive Measures

No vaccine is available; nor, at this time, are there any available drugs known to be effective as chemoprophylactic agents. Because there is no practical way for the traveler to distinguish infested from noninfested water, travelers should be advised to avoid fresh-water wading or swimming in rural areas of endemic countries. In such areas, heating bathing water to 50° Celsius (122° Fahrenheit) for 5 minutes or treating it with iodine or chlorine in a manner similar to the precautions recommended for preparing drinking water will destroy cercariae and make the water safe. Thus, swimming in adequately chlorinated swimming pools is virtually always safe, even in endemic countries. Filtering water with paper coffee filters can also be effective in removing cercariae from bathing water. If these measures are not feasible, travelers should be advised to allow bathing water to stand for 3 days because cercariae rarely survive longer than 48 hours. Vigorous towel drying after accidental exposure to water has been suggested as a way to remove cercariae in the process of skin penetration. Although toweling can prevent some infections, to recommend this to travelers might give them a false sense of security; it is far safer to recommend avoiding contact with contaminated water.

Upon return from foreign travel, those who might have been exposed to schistosome-infested fresh water should be advised to undergo screening tests.

Treatment

Safe and effective oral drugs are available for the treatment of schistosomiasis. Travelers should be advised to contact an infectious disease or tropical medicine specialist.

SEXUALLY TRANSMITTED DISEASES (STDS)

Description

Sexually transmitted diseases (STDs) are the infections and resulting clinical syndromes caused by more than 25 infectious organisms transmitted through sexual activity. Serious sequelae include pelvic inflammatory disease, infertility, stillbirths and neonatal infections, genital cancers, and (in the case of human immunodeficiency virus [HIV] and tertiary syphilis) death.

Occurrence

Acquired immunodeficiency syndrome (AIDS) has become a global health problem, and the prevalence of HIV infection in many populations continues to escalate (see the "Acquired Immunodeficiency Syndrome (AIDS)" section in this chapter, pages 57 through 59). Also of concern are the antibiotic-resistant STD agents, particularly penicillin-, tetracycline-, and quinolone-resistant strains of *Neisseria gonorrhoeae.*

Risk for Travelers

International travelers are at risk of contracting STDs, including HIV, if they have sex with partners who have these diseases. Travelers should be aware that the risk of STDs is high in some parts of the world.

Preventive Measures

Vaccine

Hepatitis B is the only STD for which a vaccine is available (see "Hepatitis, Viral, Type B," "Vaccine," this chapter, pages 93 through 95).

Other

To avoid acquiring STDs, travelers should be advised not to have sexual contact with people who might be infected. People most likely to be infected are those with numerous sex partners. In many places, people who make themselves available for sex with travelers are likely to be people, such as commercial sex workers, with many partners. In addition, injecting drug users are at high risk of being infected with HIV, regardless of the number of their sex partners.

Travelers who wish to absolutely protect themselves from acquiring an STD should be advised to refrain from sexual contact. If, however, they choose not to do this, travelers should be advised that they can reduce their risk of acquiring infection by consistently and correctly using a latex condom during sexual contact, whether vaginal, oral, or anal, as well as using a vaginal spermicide. If lubricants are used during sex, only water-based lubricants (for example, K-Y Jelly® or glycerine) should be used with latex condoms, because oil-based lubricants (for example, petroleum jelly, shortening, mineral oil, or massage oils) can weaken latex condoms.

Any traveler who might have been exposed to an STD and who develops either a vaginal or urethral discharge, an unexplained rash or genital lesion, or genital or pelvic pain should be advised to cease sexual activity and promptly seek competent medical care. Because STDs are often asymptomatic, especially in women, travelers who believe that they might have been exposed to an STD should be advised to consult a physician regarding the advisability of screening for STDs.

SMALLPOX

In May 1980, the World Health Organization (WHO) declared the global eradication of smallpox. Currently, there is no evidence of smallpox transmission anywhere in the world. The last reported case of endemic smallpox occurred in Somalia in October 1977, and the last reported case of laboratory-acquired smallpox occurred in the United Kingdom in 1978. WHO amended the International Health Regulations on January 1, 1982, deleting smallpox from the diseases subject to the regulations.

Smallpox vaccination should not be given for international travel. The risk from smallpox vaccination, although very small, now exceeds the risk of smallpox; consequently, smallpox vaccination of civilians is indicated only for laboratory workers directly involved with smallpox or closely related orthopox viruses (for example, monkeypox, vaccinia, and others). Health care workers whose contact with these viruses is limited to contaminated materials (for example, dressings) are at a lower risk of inadvertent infection than laboratory workers, but may be considered for vaccination.

Misuse of Smallpox Vaccine

Smallpox vaccine should never be used therapeutically. There is no evidence that vaccination has therapeutic value in the treatment of recurrent herpes simplex infection, warts, or any other disease.

TETANUS

(See Diphtheria, Tetanus, and Pertusis)

TUBERCULOSIS

Description

Mycobacterium tuberculosis is a rod-shaped bacterium that can cause disseminated disease, but is most frequently associated with pulmonary infections. The bacilli are transmitted by the airborne route and, depending on host factors, might or might not lead to active disease. Tuberculosis (TB) can usually be treated successfully with multiple medications.

Occurrence

In many other countries, TB is much more common than in the United States, and it is an increasingly serious public health problem.

Risk for Travelers

To become infected, a person usually would have to spend a long time in a closed environment where the air was contaminated by a person with untreated TB who was coughing and who had numerous *M. tuberculosis* organisms (or tubercle bacilli) in secretions from the lungs. TB infection is generally transmitted through the air; therefore, there is virtually no danger of its being spread by dishes, linens, and items that are touched, or by food. However, it can be transmitted through unpasteurized milk or milk products.

Travelers who anticipate possible prolonged exposure to TB (for example, those who could be expected to routinely come in contact with hospital, prison, or homeless shelter populations) should be advised to have a tuberculin skin test before leaving the United States. If the reaction is negative, they should have a repeat test after returning to the United States. Because people with human immunodeficiency virus (HIV) infection are more likely to have an impaired response to the tuberculin skin test, travelers with HIV infection should be advised to inform their physicians about their HIV status. Except for travelers with impaired immunity (for example, HIV infection), travelers who already have a positive tuberculin reaction are unlikely to be reinfected.

Centers for Disease Control and Prevention (CDC) and state and local health departments have published the results of six investigations of possible TB transmission on commercial aircraft. In these six instances, a passenger or a member of a flight crew traveled on commercial airplanes while infectious with TB. In all six instances the airlines were unaware that the passengers or crew members were infected with TB. In two of the instances, CDC concluded that TB was probably transmitted to others on the airplane. The findings suggested that the risk of TB transmission from an infectious person to others on an airplane was greater on long flights (8 hours or more). The risk of exposure to TB was higher for passengers and flight crew members sitting or working near an infectious person because they might inhale droplets containing TB bacteria.

Based on these studies and findings, the World Health Organization (WHO) issued recommendations to prevent the transmission of TB in aircraft and to guide potential investigations. The risk of TB transmission on an airplane does not appear to be greater than in any other enclosed space. To prevent the possibility of exposure to TB on airplanes, CDC and WHO recommend that people known to have infectious TB travel by private transportation (that is, not by commercial airplanes or other commercial carriers), if travel is required. CDC and WHO have issued guidelines for notifying passengers who might have been exposed to TB aboard airplanes. Passengers concerned about possible exposure to TB should be advised to see their primary health care provider for a TB skin test.

Preventive Measures

Vaccine

The Bacille Calmette-Guerin (BCG) vaccine is used in most developing countries to reduce the severe consequences of TB in infants and children. However, BCG vaccine has variable efficacy in

preventing the adult forms of TB and is, therefore, not routinely recommended for use in the United States and other developed countries.

Other

Travelers should be advised to avoid exposure to known TB patients in crowded environments (for example, hospitals, prisons, or homeless shelters). Travelers who will be working in hospitals or health care settings where TB patients are likely to be encountered should be advised to consult infection control or occupational health experts about procedures for obtaining personal respiratory protective devices (that is, N-95 respirators), along with appropriate fitting. Additionally, TB patients should be educated and trained to cover coughs and sneezes with their hands or tissues. Otherwise, no specific preventive measures can be taken or are routinely recommended for travelers.

Treatment

People who are infected or who become infected with *M. tuberculosis* can be treated to prevent TB. Recent data from the WHO suggest that isoniazid resistance is relatively common in different parts of the world. If a traveler experiences a tuberculin skin test conversion associated with international travel, consideration should be given to the possibility of drug resistance. Updated American Thoracic Society (ATS)/CDC recommendations for treatment of latent TB infection suggest that 2 months of rifampin plus pyrazinamide is a reasonable alternative to isoniazid. In settings where multidrug-resistant TB is common, experts in infectious diseases or pulmonary medicine should be consulted to determine alternative treatment regimens. Travelers who suspect that they have been exposed to TB should be advised to inform their physicians of the possible exposure and receive appropriate medical evaluation. CDC and the ATS have published updated guidelines for targeted tuberculin skin testing and treatment of latent TB infection.

TYPHOID FEVER

Description

Typhoid fever is an acute, life-threatening febrile illness caused by the bacterium *Salmonella typhi*. The disease is characterized by fever, headache, malaise, anorexia, splenomegaly, and a relative bradycardia. Many mild and atypical infections occur.

Occurrence

As estimated 16 million cases of typhoid fever and 600,000 related deaths occur worldwide. An estimated 2.6 cases of typhoid fever were reported to the Centers for Disease Control and Prevention per 1 million U.S. citizens and residents traveling abroad during the period from 1992 through 1994.

Risk for Travelers

Typhoid vaccination is not required for international travel, but it is recommended for travelers to areas where there is a recognized risk of exposure to *S. typhi*. Risk is greatest for travelers to the Indian subcontinent and to other developing countries (in Asia, Africa, and Central and South America) who will have prolonged exposure to potentially contaminated food and drink. Vaccination is particularly recommended for those who will be traveling in smaller cities, villages, and rural areas off the usual tourist itineraries. Travelers should be cautioned that typhoid vaccination is not 100% effective and is not a substitute for careful selection of food and drink.

Preventive Measures

Vaccine

Two typhoid vaccines are currently available for use in the United States: (1) an oral, live, attenuated vaccine (Vivotif Berna™ vaccine, manufactured from the Ty21a strain of *S. typhi* by the Swiss Serum and Vaccine Institute) and (2) a Vi capsular polysaccharide vaccine (ViCPS) (Typhim Vi, manufactured by Aventis Pasteur) for parenteral use. Both vaccines have been shown to protect 50% to 80% of recipients. The parenteral heat-phenol-inactivated vaccine (manufactured by Wyeth-Ayerst) has been discontinued.

Table 3-16 provides information on vaccine dosage and administration. The time required for primary vaccination differs for each of the two vaccines, and each has a different lower age limit for use among children.

Primary vaccination with oral Ty21a vaccine consists of a total of four capsules, one taken every other day. The capsules should be kept refrigerated (not frozen), and all four doses must be taken to achieve maximum efficacy. Each capsule should be taken with cool liquid no warmer than 37° Celsius (98.6° Fahrenheit), approximately one hour before a meal. The vaccine manufacturer recommends that Ty21a not be administered to infants or children younger than 6 years of age. Primary vaccination with ViCPS consists of one 0.5-milliliter (mL) (25-microgram) dose admin-istered intramuscularly. The manufacturer does not recommend the vaccine for infants younger than 2 years of age. (See Chapter 1, "Vaccination Information," "Vaccine Recommendations for Infants and Children," "Typhoid Vaccine," page 18, for a discussion of typhoid immunization for infants who will be traveling.) Current recommendations for revaccination are provided in Table 3-16.

Adverse Reactions

Information on adverse reactions is presented in Table 3-17. Information is not available on the safety of these vaccines when they are used during pregnancy; it is prudent on theoretical grounds to avoid vaccinating pregnant women. Live, attenuated Ty21a vaccine should not be given to immunocompromised travelers, including those infected with human immunodeficiency virus (HIV). The parenteral vaccine presents theoretically safer alternatives for this group. The only contraindication to vaccination with ViCPS vaccine is a history of severe local or systemic reactions

Table 3-16.—Dosage and Schedule for Typhoid Fever Vaccination.

ORAL, LIVE, ATTENUATED TY21A VACCINE					
Vaccination	**Age**	**Dose/Mode of Administration**	**Number of Doses**	**Dosing Interval**	**Boosting Interval**
Primary Series	6 years or older	1 capsule*/oral	4	48 hours	Not applicable
Booster	6 years or older	1 capsule*/oral	4	48 hours	Every 5 years
VI CAPSULAR POLYSACCHARIDE VACCINE					
Vaccination	**Age**	**Dose/Mode of Administration**	**Number of Doses**	**Dosing Interval**	**Boosting Interval**
Primary Series	2 years or older	0.50 milliliters/ Intramuscular	1	Not applicable	Not applicable
Booster	2 years or older	0.50 milliliters/ Intramuscular	1	Not applicable	Every 2 years

*Administer with cool liquid no warmer than 37° Celsius (98.6° F).

Table 3-17.—Common Adverse Reactions to Typhoid Fever.

VACCINE	REACTIONS		
	Fever	**Headache**	**Local Reactions**
Ty21A*	0%-5%	0%-5%	Not Applicable
Vi Capsular Polysaccharide	0%-1%	1.5%-3%	7% Erythema or Induration #1 cm

*The side effects of Ty21a are rare and mainly consist of abdominal discomfort, nausea, vomiting, and rash or urticaria.

following a previous dose. Neither of the available vaccines should be given to travelers with an acute febrile illness.

Precautions and Contraindications

Theoretical concerns have been raised regarding the immunogenicity of live, attenuated Ty21a vaccine in people concurrently receiving antibiotics, immune globulin, antimalarials, or viral vaccines.

The growth of the live Ty21a strain is inhibited in vitro by various antibacterial agents and by the antimalarial prophylactic agent mefloquine. Simultaneous administration of the antimalarial prophylactic agent proguanil with Ty21a vaccine resulted in significantly lower combined IgG or IgA anti-*S. typhi* lipopolysaccharide antibody response. The anti-*S. typhi* lipopolysaccharide antibody response was not significantly decreased when mefloquine was administered concurrently with Ty21a. Vaccination with Ty21a should not be administered concurrently with proguanil prophylaxis and should be delayed for more than 24 hours after the administration of any antibacterial agent or mefloquine. Chloroquine does not significantly inhibit the growth of Ty21a or the anti-*S. typhi* antibody response, and can be given concurrently. Available data do not suggest that simultaneous administration of oral polio or yellow fever vaccine decreases the immunogenicity of Ty21a. If typhoid vaccination is warranted, it should not be delayed because of the administration of viral vaccines. Simultaneous administration of Ty21a and immune globulin does not appear to pose a problem.

Other

See Chapter 4, "Health Hints for the International Traveler," "Risks From Food and Drink," pages 165 through 168.

TYPHUS FEVERS

Several distinct *Rickettsiae* species cause typhus fevers in humans. Each agent produces disease with a distinct epidemiology, but all cause illness, usually with fever, headache, or rash, or a combination of these. Treatment of all forms of typhus is similar and includes administration of appropriate antibiotics (for example, the tetracycline class) and supportive care; relapses are infrequent. Epidemic typhus is passed from person to person by the body louse. Endemic, or murine, typhus occurs worldwide and is transmitted by rat fleas. Different tickborne typhus fevers occur in Europe, Africa, the Americas, Australia, and Asia. Scrub typhus, transmitted by rodent mites, occurs in a large area from the Indian subcontinent to Australia and in much of Asia, including Japan, China, Korea, and parts of Russia.

Occurrence

Endemic typhus is common year round in the tropics. In temperate areas, it occurs during the summer months when rats and their fleas are most active and abundant. Outbreaks of epidemic typhus are rare except during periods when normal hygiene is disrupted, as in refugee camps arising from wars or natural disasters. It also occurs in some populations living in higher elevations during the colder months when louse-infested clothing is not laundered and person-to-person spread of lice is common. Scrub typhus can occur throughout the year, but is dependent on temperature and rainfall (which affect the prevalence of the mites that transmit the disease).

Risk for Travelers

Endemic typhus occurs often in people frequenting rat-infested buildings and houses in harbor or riverine areas. Foci of epidemic typhus exist in impoverished and dislocated populations in the highlands of some parts of Africa and South America, but travelers are rarely at risk of acquiring lice and disease. Scrub typhus and tick typhus occur in people who engage in occupational or recreational behaviors that bring them inadvertently in contact with mite- or tick-infested habitats that harbor the rodent hosts of these arthropods. Tick typhus infections, often called spotted fevers, occur occasionally in travelers who spend time in nature trekking or camping, or on safari.

Preventive Measures

Vaccine

Vaccination against any of the typhus fevers is not required by any country as a condition for entry. Although experimental vaccines have been developed for the typhus fevers, no commercially licensed vaccines are produced presently in the United States.

Other

Travelers should be advised that prevention is based on avoidance of vector-infested habitats, use of repellents and protective clothing when exposed, prompt detection and removal of arthropods on clothing and skin, and attention to hygiene. Disease management should focus on early detection and proper treatment to prevent severe complications of these illnesses.

VARICELLA (CHICKENPOX)

Description

Varicella is an acute, highly communicable viral disease caused by varicella zoster virus (VZV). The first infection with VZV results in varicella (chickenpox), which presents as a generalized vesicular rash. The virus becomes latent in sensory nerve ganglia and can recur later in life. Recurrent disease with VZV results in herpes zoster (shingles), usually localized to one to three dermatomes. Transmission of VZV to a susceptible person occurs through contact with either a person with varicella or, less commonly, a person with zoster. Varicella is generally a mild disease in infants and children, but can result in secondary bacterial infections of skin lesions, pneumonia, cerebellar ataxia, and encephalitis. Adults are at a higher risk for complications than are children.

Occurrence

Varicella is endemic in the United States and virtually all people have been infected by adulthood. Incidence is expected to decline as vaccine coverage levels increase. The majority of cases (approximately 85%) occur among infants, children, and adolescents younger than 15 years of age. In recent years, the highest incidence has been among infants and children 1 through 4 years of age (100.4 cases per 1,000 infants and children), and is probably the result of early exposure to VZV in preschool and child care settings. Children 5 through 9 years of age have an age-specific incidence of 91 cases per 1,000 children. Adults 20 years of age or older have a very low incidence rate (approximately 1.5 cases per 1,000 persons) and account for approximately 5% of cases.

Risk for Travelers

Varicella and herpes zoster occur worldwide, and the vaccine is routinely used in very few countries. The risk of varicella to the traveler is as high in the United States as anywhere else in the world. Data suggest that varicella infection is less common in infancy and childhood in tropical areas, where chickenpox occurs more commonly among adults. The reasons for this difference in age distribution are not known with certainty, but are believed to be due to the lack of infancy and childhood varicella exposure in rural populations or to the heat lability of the virus, or both.

Preventive Measures

Vaccine

Varicella vaccine contains live, attenuated varicella zoster virus. It is currently available only as a single-antigen formulation. After one dose of varicella vaccine, 97% of infants and children 1 through 12 years of age develop detectable antibody titers. Vaccine-induced immunity is believed to be long-lasting. Vaccine efficacy is estimated to be 90% against VZV infection and 95% against severe disease. Among healthy adolescents and adults, an average of 78% develop antibody after one dose and 99% develop antibody after a second dose given 4 to 8 weeks later.

Although vaccination against varicella is not a requirement for entry into any country (including the United States), people traveling or living abroad should be advised to ensure that they are immune. In general, people can be considered immune to varicella if they have a reliable personal history of varicella, laboratory (serologic) evidence of varicella immunity, or proof of receipt of one or two doses of varicella vaccine (depending on the age of vaccination) on or after their first birthday.

One dose of varicella virus vaccine is recommended for all infants without contraindications at 12 to 18 months of age. The vaccine may be given to infants and children at this age regardless of their prior history of varicella. However, immunization is not necessary in infants and children with reliable histories of chickenpox. A prior history of chickenpox is not a contraindication to varicella vaccination. Infants younger than 12 months of age will generally be protected from varicella because of passive maternal antibody.

Varicella vaccine is recommended for susceptible children, adolescents, and adults. Infants and children 1 through 12 years of age should receive one dose. Those 13 years of age or older should receive two doses of vaccine 4 to 8 weeks apart. Children, adolescents, and adults with reliable parental or personal histories of chickenpox can be assumed to be immune. Those without a reliable history can be considered to be susceptible. Epidemiologic and serologic studies indicated that >95% of American adults are immune to varicella. In addition, 71% to 93% of adults without a reliable history of chickenpox are actually immune. As a result, serologic testing prior to vaccination is likely to be cost effective for adults. As with infants and children, a prior history of chickenpox is not a contraindication to varicella vaccination.

Varicella vaccine may be administered simultaneously (but in a different site) with any other live or inactivated vaccine. Inactivated vaccines and typhoid vaccines may be administered at any time before or after varicella vaccine. However, if varicella vaccine or live measles, mumps, and rubella (MMR) and yellow fever vaccines are not administered simultaneously, their administration should be separated by an interval of at least 28 days. (See Chapter 1, "Vaccination Information," "U.S. Public Health Service Recommendations," pages 6 through 12, for more details.)

Adverse Reactions

The most common adverse reactions following varicella vaccine are injection site complaints such as pain, soreness, redness, and swelling. Based on information from the manufacturer's clinical trials of varicella vaccine, local reactions are reported in 19% of infants and children and 24% of adolescents and adults (33% following the second dose). These local adverse events are generally mild and self-limited. A varicella-like rash at the injection site is reported in 3% of infants and children and in 1% of adolescents and adults following the second dose. In both groups, there is a median of two lesions. These lesions generally occur within 2 weeks of vaccination and are most commonly maculopapular rather than vesicular.

A generalized varicella-like rash is reported in 4% to 6% or recipients of varicella vaccine (1% after the second dose in adolescents and adults), with a median of five lesions. Most of these generalized rashes occur within 3 weeks of vaccination, most are maculopapular, and not all are attributable to the vaccine.

Fever within 42 days of vaccination is reported in 15% of infants and children and 10% of adolescents and adults. The majority of these episodes of fever have been attributed to intercurrent illness rather than to the vaccine.

Varicella vaccine is a live virus vaccine and results in a latent infection similar to that caused by wild varicella virus. Consequently, zoster caused by the vaccine virus has been reported. To date, fewer than 50 reports of zoster with submitted laboratory specimens in vaccinated people, mostly infants and children, have been received out of more than 250 reports received through July 1998. Not all these cases have been confirmed as having been caused by vaccine virus and many were caused by the wild virus.

Precautions and Contraindications

Allergy.—People with severe allergy (that is, hives, swelling of the mouth or throat, difficulty breathing, hypotension, and shock) to gelatin or neomycin or who have had a severe allergic reaction to a prior dose should generally not be vaccinated with varicella vaccine. Varicella vaccine does not contain egg protein or preservative.

Pregnancy.—Women known to be pregnant or attempting to become pregnant should not receive varicella vaccine. The effects of varicella vaccine on a developing fetus are unknown. Because infection with wild varicella virus poses only a small risk to the fetus and the vaccine virus is attenuated, the risk to the fetus, if any, should be even lower. Although the manufacturer's package insert states otherwise, the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics recommend that pregnancy be avoided for one month following receipt of varicella vaccine. Breast-feeding is not a contraindication to the varicella vaccination of either a woman or an infant. Varicella vaccination has no known effect on antibiotics, and these drugs are not known to reduce the immunogenicity of the vaccine.

Immunosuppression.—People with immunosuppression of cellular immune function resulting from leukemia, lymphoma, generalized malignancy, immune deficiency disease, or immunosuppressive therapy should not be vaccinated. However, the vaccine may, under a research protocol, be given to infants and children with leukemia in remission who fulfill certain eligibility criteria. However, treatment with low-dose (<2 milligrams per kilogram per day [mg/kg/day] or <20 mg/day of prednisone), alternate-day, topical-replacement, or aerosolized steroid preparations is not a contraindication to varicella vaccination. People whose immunosuppressive therapy with steroids has been stopped for 1 month (3 months for chemotherapy) may be vaccinated. In addition, people with impaired humoral immunity may now be vaccinated. Because infants and children infected with human immunodeficiency virus (HIV) are at increased risk for morbidity from varicella and herpes zoster (that is, shingles) compared with healthy infants and children, the ACIP recommends that, after weighing potential risks and benefits, varicella vaccine should be considered for asymptomatic or mildly symptomatic HIV-infected infants and children in CDC class N1 (no signs or symptoms) or A1 (mild signs or symptoms) with age-specific CD4+ T-lymphocyte percentages of $25%. Eligible infants and children should receive two doses of varicella vaccine, with a 3-month interval between doses. The use of varicella vaccine in other HIV-infected children is being investigated further.

Acute Illness.—Vaccination of people with moderate or severe acute illness should be postponed until their condition has improved. Minor illnesses, such as upper respiratory infections with or without low-grade fever, do not preclude vaccination.

Recent Administration of Immune Globulin (IG) or Other Antibody-Containing Blood Products.—The effect of the administration of antibody-containing blood products (for example, IG, whole blood or packed red blood cells, intravenous IG, or varicella zoster IG [VZIG]) on the response to varicella vaccine virus is unknown. Because of the potential inhibition of the response to varicella vaccination by passively transferred antibodies, varicella vaccine should not be given for at least 5 months after antibody-containing blood products are given. IG or VZIG should not be given

for 3 weeks following vaccination unless its benefits exceed those of the vaccine. In such cases, the vaccinees should either be revaccinated 5 months later or be tested for immunity 6 months later and revaccinated if seronegative.

No adverse events following varicella vaccination related to the use of salicylates (for example, aspirin) have been reported to date. However, the manufacturer recommends that vaccine recipients avoid the use of salicylates for 6 weeks after receiving varicella vaccine because of the association between aspirin use and Reye's syndrome following chickenpox.

The effect of varicella vaccine, if any, on tuberculin testing is unknown. However, measles vaccine (and possibly mumps and rubella vaccines) can suppress the response to purified protein derivative (PPD) in a person infected with *Mycobacterium tuberculosis*. Until additional information is available, it is prudent to apply the same procedures for PPD and measles vaccination to varicella vaccine. If PPD testing is needed, it should be done prior to MMR or varicella vaccination. PPD testing should be delayed for 4 to 6 weeks after MMR or varicella vaccination. It is also acceptable to apply the PPD and administer MMR or varicella, or both, simultaneously.

The effect of varicella vaccine on antimalarial drugs is not known; therefore, it is prudent to administer varicella vaccine before commencing antimalarial prophylaxis if possible.

YELLOW FEVER

Description

Yellow fever is a mosquito-borne viral disease. Illness varies in severity from a flu-like syndrome to severe hepatitis and hemorrhagic fever.

Occurrence

The disease occurs only in sub-Saharan Africa (where it is endemic) and tropical South America (see Maps 3-6 through 3-7.) In Africa, a variety of vectors are responsible for the disease and it is in Africa where the majority of the cases are reported. The case fatality rate is approximately 23%, and infants and children are at greatest risk for infection. In South America, cases occur most frequently in young men who have an occupational exposure to the vector in forested or transitional areas of Bolivia, Brazil, Colombia, Ecuador, and Peru. The case fatality rate is approximately 65%.

Risk for Travelers

Although yellow fever has rarely occurred in travelers, fatal cases of yellow fever have occurred in some unvaccinated travelers visiting rural areas within the yellow fever endemic zone.

Table 3-18.—Yellow Fever Vaccine.

DOSES	DOSE VOLUME*	COMMENTS
Primary:1	0.5 milliliters	Not applicable
Booster	0.5 milliliters	1 dose every 10 years

*Older than 9 months of age.

Preventive Measures

Vaccine

Yellow fever is preventable by a safe, effective vaccine (see Table 3-18 for dosage information). International regulations require proof of vaccination for travel to and from certain countries. For purposes of international travel, vaccines produced by different manufacturers worldwide must be approved by the World Health Organization and administered at an approved yellow fever vaccination center. State and territorial health departments have authority to designate nonfederal vaccination centers; these can be identified by contacting state or local health departments. (The Centers for Disease Control and Prevention [CDC] does not maintain a list of the designated centers.) Vaccinees should receive an international certificate of vaccination completed, signed, and validated with the center's stamp where the vaccine was given.

A number of countries require a certificate from travelers arriving from infected areas or from countries with infected areas. Some countries in Africa require evidence of vaccination from all entering travelers; others may waive the requirements for travelers coming from noninfected areas and staying in the country less than 2 weeks.

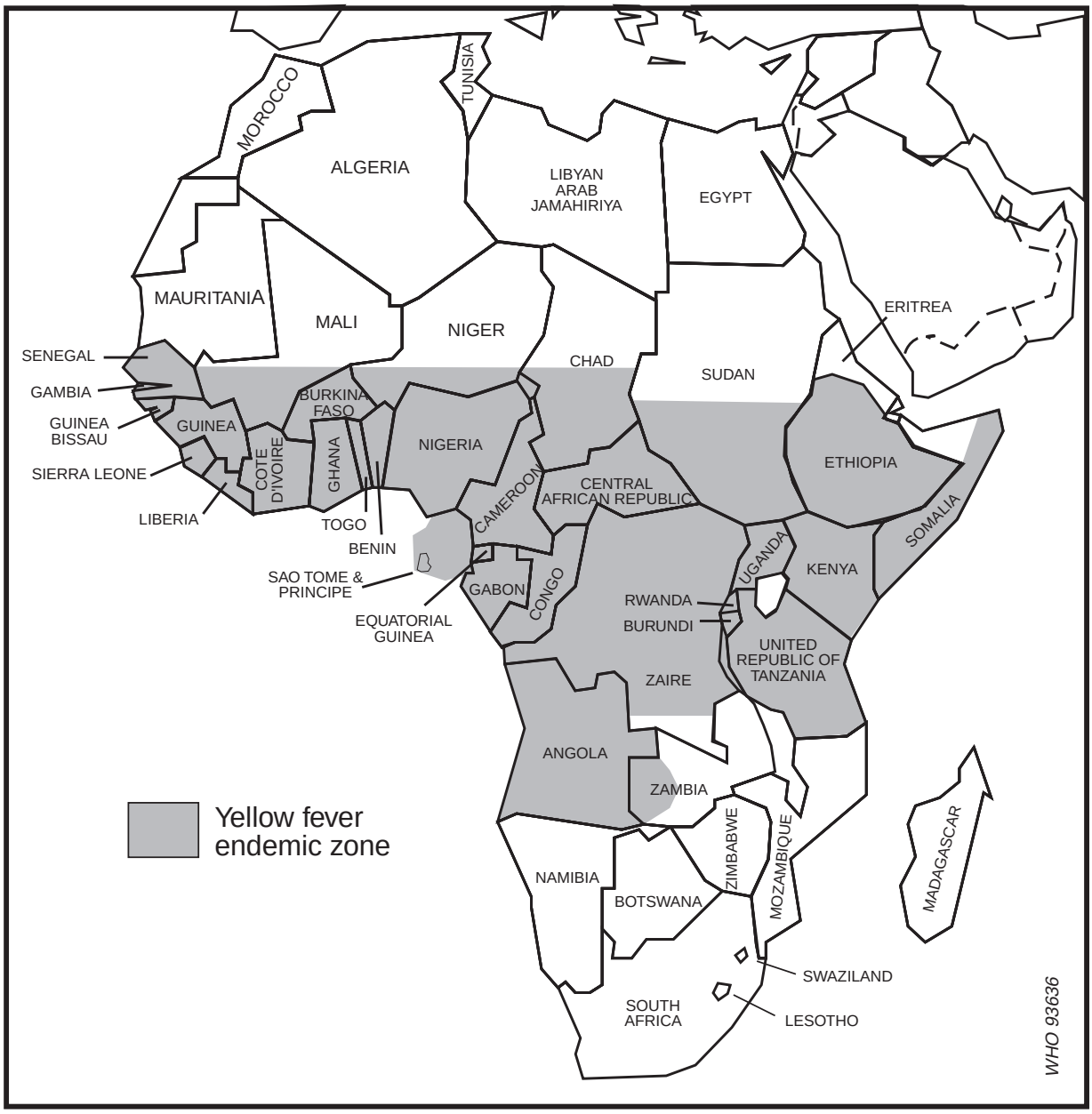
Vaccination is also recommended for travel outside the urban areas of countries that do not officially report the disease, but which lie in the yellow fever endemic zone (see Maps 3-6 and 3-7). It should be noted that the actual areas of yellow fever virus activity can extend beyond the officially reported infected zones.

Some countries require a traveler, even if only in transit, to have a valid international certificate of vaccination if he or she has been in any country either known or thought to harbor yellow fever virus. Such requirements may be strictly enforced, particularly for people traveling from Africa or South America to Asia. Travelers with a specific contraindication to yellow fever vaccine should be advised to obtain a waiver before traveling to countries requiring vaccination. (See "Precautions and Contraindications" in this section, pages 158 and 159).

Adverse Reactions

Reactions to yellow fever vaccine are generally mild. From 2% to 5% of vaccinees have mild headaches, myalgia, low-grade fevers, or other minor symptoms 5 to 10 days after vaccination. Fewer

Yellow Fever Endemic Zones in Africa



NOTE: Although the "yellow fever endemic zones" are no longer included in the International Health Regulations, a number of countries (most of them not bound by the Regulations or bound with reservations) consider these zones as infected areas and require an International Certificate of Vaccination against Yellow Fever from travelers arriving from those areas. The above map based on information from WHO is therefore included in this publication for practical reasons.

Map 3-7.—Yellow Fever Endemic Zones in the Americas, 2000.

Yellow Fever Endemic Zone

Note: Although the "yellow fever endemic zones" are no longer included in the International Health Regulations, a number of countries (most of them not bound by the regulations or bound with reservations) consider the zones shown as infected areas and require an international certificate of vaccination against yellow fever from travelers arriving from those areas. This map, based on information from the World Health Organization (WHO-99347), is included in this publication for practical reasons.

than 0.2% of vaccinees find it necessary to curtail regular activities. Immediate hypersensitivity reactions, characterized by rash, urticaria, or asthma, or a combination of these, are extremely uncommon (incidence less than 1 case per 1,000,000 vaccinees) and occur principally in people with histories of egg allergy.

Precautions and Contraindications

Age.—The risk of adverse reactions appears to be age related. Infants younger than 4 months of age are more susceptible to serious adverse reactions (encephalitis) than older infants and children and should not be immunized. Immunization should be delayed until an infant is at least 9 months of age. (See Chapter 1, "Vaccination Information, "Vaccine Recommendations for Infants and Children," "Yellow Fever Vaccine," page 21, for a discussion of yellow fever immunization for infants and children.)

A recent analysis of adverse events passively reported to the Vaccine Adverse Event Reporting System (VAERS) during the period 1990 through 1998 suggests that people 65 years of age or older might be at increased risk for a variety of systemic adverse events following vaccination compared with people 25 through 44 years of age. Among civilians administered an estimated 1.5 million doses of yellow fever vaccine during this 9-year period, there were four cases (63, 67, 76, and 79 years of age) of severe illness with fever and multisystem viscerotropic manifestations characteristic of vaccine-induced yellow fever. In Brazil, during an ongoing mass vaccination campaign in which 34 million doses of Brazilian-manufactured yellow fever vaccine (a different vaccine strain than that used in the United States) have been administered since 1998, two similar cases (although 5 and 22 years of age) have recently been reported. Additional studies are now underway to better define the cause and risk factors for these rare, but significant, adverse events associated with two different yellow fever vaccines.

Yellow fever remains an important cause of illness and death in sub-Saharan Africa. In South American, the number of reported cases of yellow fever has increased dramatically and the potential yellow fever transmission zone has expanded to urban areas with large populations of susceptible humans and the *Aedes aegyptii* vector mosquito, thus threatening to reestablish the urban cycle of yellow fever transmission. For the first time in decades, unvaccinated U.S. travelers to South America have contracted fatal yellow fever. Consequently, despite the reported adverse events, which are exceedingly rare, yellow fever vaccination in endemic areas and of travelers should generally be encouraged as an important prevention strategy. Elderly travelers should be encouraged to discuss with their physicians the risks and benefits of vaccination in the context of the destination-specific risk for exposure to yellow fever.

Pregnancy.—A small study showed that yellow fever vaccine virus given in pregnancy can infect the developing fetus, but the potential risk of adverse events associated with congenital infection is unknown. Therefore, it is prudent to avoid vaccinating pregnant women and for nonimmunized pregnant women to postpone travel to transmission areas until after delivery. If the travel itinerary of a pregnant woman does not present a substantial risk of exposure and immunization is contemplated solely to comply with an international travel requirement, then the traveler should be advised to obtain a waiver letter from her physician. Pregnant women who must travel to areas with

active, ongoing transmission should be vaccinated. It is believed that under these circumstances, the small theoretical risk for mother and fetus from vaccination is far outweighed by the risk of yellow fever infection.

Immunosuppression.—Infection with yellow fever virus poses a theoretical risk to travelers with immunosuppression in association with acquired immunodeficiency syndrome (AIDS) or other manifestations of human immunodeficiency virus (HIV) infection, leukemia, lymphoma, or generalized malignancy; or with the administration of corticosteroids, alkylating drugs, antimetabolites, or radiation. There are no anecdotal reports or systematically collected data, however, linking an immunosuppressed state with adverse events in a yellow fever vaccine recipient. The decision to immunize immunocompromised travelers with yellow fever vaccine should be based on a physician's evaluation of the traveler's state of immunosuppression weighed against the risk of exposure to the virus. If travel to a yellow fever-infected zone is necessary and immunization is contraindicated, a traveler should be advised of the risk, instructed in methods to avoid bites of vector mosquitoes, and supplied a vaccination waiver letter by his or her physician. Anecdotal experience suggests that low-dose (10 milligrams of prednisone or equivalent daily) or short-term (less than 2 weeks) corticosteroid therapy, or intra-articular, bursal, or tendon injections with corticosteroid do not pose a risk to recipients of yellow fever vaccine. Travelers with asymptomatic HIV infections who cannot avoid potential exposure to yellow fever virus should be offered the choice of immunization. If vaccinated, they should be monitored for possible adverse effects. Because immunization for these travelers might be less effective than for uninfected travelers, the neutralizing antibody response should be measured following vaccination prior to travel. Physicians should consult the applicable state health department or CDC, Fort Collins, Colorado, 1-970-221-6400, for more information.

Family members or close contacts of immunosuppressed travelers, who themselves have no contraindications, may receive yellow fever vaccine.

Hypersensitivity.—Live yellow fever vaccine is produced in chick embryos and should not be given to travelers clearly hypersensitive to eggs; generally, people who are able to eat eggs or egg products may receive the vaccine. If vaccination of a person with a questionable history of egg hypersensitivity is considered essential because of a high risk of exposure, an intradermal test dose may be administered under close medical supervision. Specific directions for skin testing are found in the package insert. In some instances, small test doses for vaccine administered intradermally have led to an antibody response.

If international travel regulations are the only reason to vaccinate a traveler hypersensitive to eggs, efforts should be made to obtain a waiver. A physician's letter clearly stating the contraindications to vaccination is acceptable to some governments. (Ideally, it should be written on letterhead stationary and bear the stamp used by health department and official immunization centers to validate the international certificate of vaccination.) Under these conditions, it is also useful for the traveler to obtain specific and authoritative advice from the embassy or consulate of the country or countries he or she plans to visit. Waivers of requirements obtained from embassies or consulates should be documented by appropriate letters and retained for presentation with the international certificate of vaccination.

Simultaneous Administration of Other Vaccines and Drugs.—Studies have shown that the seroimmune response to yellow fever vaccine is not inhibited by administration of certain other vaccines concurrently or at various intervals of a few days to one month. Measles and Bacille Calmette-Guerin (BCG) have been administered in combination with yellow fever vaccines without interference. Additionally, the severity of reactions to vaccination has not been amplified by concurrent administration of yellow fever and measles vaccines. Hepatitis B and yellow fever vaccines may be given concurrently. If live virus vaccines are not given concurrently, 4 weeks should be allowed to elapse between sequential vaccinations.

There are no data on possible interference between yellow fever and typhoid, rabies, or Japanese encephalitis vaccines.

A prospective study of people given yellow fever vaccine and 5 milliliters of commercially available immune globulin revealed no alteration of the immunologic response to yellow fever vaccine when compared with controls. Although chloroquine inhibits replication of yellow fever virus in vitro, it does not adversely affect antibody responses to yellow fever vaccine in people receiving the drug as antimalarial prophylaxis.

Other

In addition to vaccination, travelers should be advised to take precautions against exposure to mosquitoes when traveling in areas with yellow fever transmission. Yellow fever is rarely transmitted in urban areas, except during an epidemic. Travelers to rural areas of Africa and South America, however, might be exposed sporadically to mosquitoes transmitting yellow fever and other mosquito-borne diseases. Mosquitoes that transmit urban yellow fever generally feed during the day, both indoors and outdoors. Staying in air-conditioned or well-screened quarters and wearing long-sleeved shirts and long pants will help to prevent mosquito bites. Insect repellents containing N,N-diethylmetatoluamide (DEET) should be used on exposed skin only. Permethrin-containing repellents should be applied to clothing. Travelers to rural areas should bring mosquito nets and aerosol insecticides or mosquito coils. (For further prevention information, see Chapter 4, “Health Hints for the International Traveler,” “Protection Against Mosquitoes and Other Arthropod Vectors,” pages 163 through 165.)

CHAPTER 4

HEALTH HINTS FOR THE INTERNATIONAL TRAVELER

INTRODUCTION

This section includes practical information on how the traveler can avoid potential health problems. Some of these recommendations are common sense precautions; others have been scientifically documented.

Personal and specific preventive measures against certain diseases might require advance planning and advice from a physician or the local health department concerning immunization and prophylaxis.

Travelers who take prescription medications should be advised to carry an adequate supply, accompanied by a signed and dated statement from a physician; the statement should indicate the major health problems and dosages of such medications to provide information for medical authorities in case of emergency. As applicable, travelers should also be advised to take an extra pair of glasses or lens prescription and a card, tag, or bracelet that identifies any physical condition that might require emergency care.

MOTION SICKNESS

Travelers with a history of motion sickness can attempt to avoid symptoms by taking anti-motion-sickness medications (for example, antihistamines) before departure.

PROTECTION AGAINST MOSQUITOES AND OTHER ARTHROPOD VECTORS

Although vaccines or chemoprophylactic drugs are available against important vector-borne diseases such as yellow fever and malaria, there are none for most other mosquito-borne diseases such as dengue, and travelers still should be advised to use repellents and other general protective measures against arthropods. The effectiveness of malaria chemoprophylaxis is variable, depending on patterns of resistance and compliance with medication. For many vector-borne diseases, no specific preventatives are available.

General Preventive Measures

The principal approach to prevention of vector-borne diseases is avoidance. Tick- and mite-borne infections characteristically are diseases of “place”; whenever possible, known foci of disease transmission should be avoided. Although many vector-borne infections can be prevented by avoiding rural locations, certain mosquito- and midge-borne arboviral and parasitic infections are transmitted seasonally, and simple changes in itinerary can greatly reduce risk for acquiring certain infections.

Travelers should be advised that exposure to arthropod bites can be minimized by modifying patterns of activity or behavior. Some vector mosquitoes are most active in twilight periods at dawn and dusk or in the evening. Avoidance of outdoor activity during these periods can reduce risk of exposure. Wearing long-sleeved shirts, long pants, and hats will minimize areas of exposed skin. Shirts should be tucked in. Repellents applied to clothing, shoes, tents, mosquito nets, and other gear will enhance protection.

When exposure to ticks or biting insects is a possibility, travelers should be advised to tuck their pants into their socks and to wear boots, not sandals. Permethrin-based repellents applied as directed (see the following section, "Repellents") will enhance protection. Travelers should be advised that, during outdoor activity and at the end of the day, they should inspect themselves and their clothing for ticks. Ticks are detected more easily on light-colored or white clothing. Prompt removal of attached ticks can prevent some infections.

When accommodations are not adequately screened or air conditioned, bed nets are essential to provide protection and comfort. Bed nets should be tucked under mattresses and can be sprayed with a repellent, such as permethrin. The permethrin will be effective for several months if the bed net is not washed. Aerosol insecticides and mosquito coils can help to clear rooms of mosquitoes; however, some coils contain dichlorodiphenyltrichloroethane (DDT) and should be used with caution.

Repellents

Travelers should be advised that permethrin-containing repellents (such as Permanone®) are recommended for use on clothing, shoes, bed nets, and camping gear. Permethrin is highly effective as an insecticide and acaricide and as a repellent. Permethrin-treated clothing repels and kills ticks, mosquitoes, and other arthropods, and retains this effect after repeated laundering. There appears to be little potential for toxicity from permethrin-treated clothing. The insecticide should be reapplied after every five washings.

Permethrin-containing shampoo (Nix®) and cream (Elimite®), marketed for use against head lice and scabies infestations, potentially could be effective as repellents when applied on the hair and skin. However, they are approved only to treat existing conditions. Most authorities recommend repellents containing N,N-diethylmetatoluamide (DEET) as an active ingredient. DEET repels mosquitoes, ticks, and other arthropods when applied to the skin or clothing. Formulations containing <35% DEET are recommended because the additional gain in repellent effect with higher concentrations is not significant when weighed against the potential for toxicity. Travelers should be advised to use lower concentrations for children (no more than 10% DEET). Repellents with DEET should be used sparingly on children 2 through 6 years of age and not at all on infants younger than 2 years of age. A microencapsulated, sustained release formulation can have a longer period of activity than liquid formulations at the same concentrations. Length of protection also varies with ambient temperature, extent of perspiration, any water exposure, abrasive removal, and other factors.

DEET is toxic when ingested. High concentrations applied to skin can cause blistering. Rare cases of encephalopathy in children, some fatal, have been reported after cutaneous exposure. Other neurologic side effects also have been reported. Toxicity did not appear to be dose-related in many cases and these might have been idiosyncratic reactions in predisposed individuals. However, a dose-related effect leading to irritability and impaired concentration and memory has been reported.

Travelers should be advised that the possibility of adverse reactions to DEET will be minimized if they take the following precautions: (1) apply repellent sparingly and only to exposed skin or clothing; (2) avoid applying high-concentration products to the skin; (3) do not inhale or ingest repellents or get them in the eyes; (4) avoid applying repellents to portions of children's hands that are likely to have contact with the eyes or mouth; (5) never use repellents on wounds or irritated skin; and (6) wash repellent-treated skin after coming indoors. If a reaction to insect repellent is suspected, travelers should be advised to wash treated skin and seek medical attention.

Bed nets, repellents containing DEET, and permethrin should be purchased before traveling and can be found in hardware, camping, sporting goods, and military surplus stores.

RISKS FROM FOOD AND DRINK

Contaminated food and drink are common sources for the introduction of infection into the body. Among the more common infections that travelers can acquire from contaminated food and drink are *Escherichia coli* infections, shigellosis or bacillary dysentery, giardiasis, cryptosporidiosis, and hepatitis A. Other less common infectious disease risks for travelers include typhoid fever and other salmonelloses, cholera, infections caused by rotavirus and Norwalk-like viruses, and a variety of protozoan and helminthic parasites (other than those that cause giardiasis and cryptosporidiosis). Many of the infectious diseases transmitted in food and water can also be acquired directly through the fecal-oral route.

Water

Water that has been adequately chlorinated, using minimum recommended water treatment standards employed in the United States, will afford significant protection against viral and bacterial waterborne diseases. However, chlorine treatment alone, as used in the routine disinfection of water, might not kill some enteric viruses and the parasitic organisms that cause giardiasis, amebiasis, and cryptosporidiosis. In areas where chlorinated tap water is not available or where hygiene and sanitation are poor, travelers should be advised that only the following might be safe to drink:

1. Beverages, such as tea and coffee, made with boiled water.

2. Canned or bottled carbonated beverages, including carbonated bottled water and soft drinks.

3. Beer and wine.

Where water might be contaminated, travelers should be advised that ice should also be considered contaminated and should not be used in beverages. If ice has been in contact with containers used for drinking, travelers should be advised to thoroughly clean the containers, preferably with soap and hot water, after the ice has been discarded.

It is safer to drink a beverage directly from the can or bottle than from a questionable container. However, water on the outside of beverage cans or bottles might be contaminated also. Therefore, travelers should be advised to dry wet cans or bottles before they are opened, and to wipe clean surfaces with which the mouth will have direct contact. Where water might be contaminated, travelers should be advised to avoid brushing their teeth with tap water.

Treatment of Water

Travelers should be advised of the following methods for treating water to make it safe for drinking and other purposes.

Boiling is by far the most reliable method to make water of uncertain purity safe for drinking. Water should be brought to a vigorous rolling boil for 1 minute and allowed to cool to room temperature; ice should not be added. This procedure will kill bacterial and parasitic causes of diarrhea at all altitudes and viruses at low altitudes. To kill viruses at altitudes above 2,000 meters (6,562 feet), water should be boiled for 3 minutes or chemical disinfection should be used after the water has boiled for 1 minute. Adding a pinch of salt to each quart or pouring the water several times from one clean container to another will improve the taste.

Chemical disinfection with iodine is an alternative method of water treatment when it is not feasible to boil water. However, this method cannot be relied upon to kill *Cryptosporidium* unless the water is allowed to sit for 15 hours before it is drunk. Two well-tested methods for disinfection with iodine are the use of tincture of iodine (Table 4-1) and the use of tetraglycine hydroperiodide tablets (for example, Globaline®, Potable-Aqua®, or Coghlan's®). These tablets are available from pharmacies and sporting goods stores. The manufacturers' instructions should be followed. If water is cloudy, the number of tablets used should be doubled; if water is extremely cold (#5° Celsius [#41° Fahrenheit]), an attempt should be made to warm the water, and the recommended contact time should be increased to achieve reliable disinfection. Cloudy water should be strained through a clean cloth into a container to remove any sediment or floating matter, and then the water should be boiled or treated with iodine. Chlorine, in various forms, can also be used for chemical disinfection. However, its germicidal activity varies greatly with the pH, temperature, and organic content of the water to be purified and, therefore, it can produce less consistent levels of disinfection in many types of water. Chemically treated water is intended for short-term use only. If iodine-disinfected water is the only water available, it should be used for only a few weeks.

Portable filters currently on the market will provide various degrees of protection against microbes. Reverse-osmosis filters provide protection against viruses, bacteria, and protozoa, but they are expensive, are larger than most filters used by backpackers, and the small pores on this type of filter are rapidly plugged by muddy or cloudy water. In addition, the membranes in some filters can be

Table 4-1.—Treatment of Water With Tincture of Iodine.

TINCTURE OF IODINE	DROPS* TO BE ADDED PER QUART OR LITER	
	Clear Water	**Cold or Cloudy Water†**
2%	5	10

Note: tincture of iodine can come from a medicine chest or first-aid kit.
*1 drop = 0.05 milliliter. Water must stand for a minimum of 30 minutes before it is safe to use.
†Very turbid or very cold water can require prolonged contact time; if possible, such water should be allowed to stand several hours prior to use. To ensure that *Cryptosporidium* is killed, water must stand for 15 hours before drinking.

damaged by chlorine in water. Microstrainer filters with pore sizes in the 0.1- to 0.3-micrometer range can remove bacteria and protozoa from drinking water, but they do not remove viruses. To kill viruses, travelers using microstrainer filters should be advised to disinfect the water with iodine or chlorine after filtration, as described previously. Filters with iodine-impregnated resins are most effective against bacteria, and the iodine will kill some viruses; however, the contact time with the iodine in the filter is too short to kill the protozoa *Cryptosporidium* and, in cold water, *Giardia*. Proper selection, operation, care, and maintenance of water filters is essential to producing safe water. The manufacturers' instructions should be followed. NSF International, an independent testing company, tests and certifies water filters for their ability to remove protozoa, but not for their ability to remove bacteria or viruses. Few published reports in the scientific literature have evaluated the efficacy of specific brands or models of filters against bacteria and viruses in water. Until such information becomes available, the Centers for Disease Control and Prevention (CDC) cannot identify which specific brands or models of filters are most likely to remove bacteria and viruses. A list of filters that have passed NSF tests for parasite removal can be obtained by calling 1-800-673-8010; by writing to NSF at 789 North Dixboro Road, P.O. Box 130140, Ann Arbor, Michigan 48113-0140; or online at http://www.NSF.org.

As a last resort, if no source of safe drinking water is available or can be obtained, tap water that is uncomfortably hot to touch might be safer than cold tap water; however, proper disinfection, filtering, or boiling is still advised.

Food

To avoid illness, travelers should be advised to select food with care. All raw food is subject to contamination. Particularly in areas where hygiene and sanitation are inadequate, the traveler should be advised to avoid salads, uncooked vegetables, and unpasteurized milk and milk products such as cheese, and to eat only food that has been cooked and is still hot, or fruit that has been peeled by the traveler personally. Undercooked and raw meat, fish, and shellfish can carry various intestinal pathogens. Cooked food that has been allowed to stand for several hours at ambient temperature can provide a fertile medium for bacterial growth and should be thoroughly reheated before serving. Consumption of food and beverages obtained from street food vendors has been associated with an

increased risk of illness. The easiest way to guarantee a safe food source for an infant younger than 6 months of age is to have the infant breast feed. If the infant has already been weaned from the breast, formula prepared from commercial powder and boiled water is the safest and most practical food.

Some species of fish and shellfish can contain poisonous biotoxins, even when well cooked. The most common type of biotoxin in fish is ciguatoxin. The flesh of the barracuda is the most toxic laden and should always be avoided. Red snapper, grouper, amberjack, sea bass, and a wide range of tropical reef fish contain the toxin at unpredictable times. The potential for ciguatera poisoning exists in all subtropical and tropical insular areas of the West Indies and the Pacific and Indian Oceans where the implicated fish species are eaten. Symptoms of ciguatera poisoning include gastroenteritis followed by neurologic problems such as dysesthesias; temperature reversal; weakness; and, rarely, hypotension. Scombroid is another common fish poisoning that occurs worldwide in tropical, as well as temperate, regions. Fish of the Scombridae family (for example, bluefin, yellowfin tuna, mackerel, and bonito), as well as some nonscombroid fish (for example, mahimahi, herring, amberjack, and bluefish) may contain high levels of histidine in their flesh. With improper refrigeration or preservation, histidine is converted to histamine, which can cause flushing, headache, nausea, vomiting, diarrhea, and urticaria.

Cholera cases have occurred among people who ate crab brought back from Latin America by travelers. Travelers should be advised not to bring perishable seafood with them when they return to the United States from high-risk areas.

TRAVELERS' DIARRHEA

Epidemiology

Travelers' diarrhea (TD) is a syndrome characterized by a twofold or greater increase in the frequency of unformed bowel movements. Commonly associated symptoms include abdominal cramps, nausea, bloating, urgency, fever, and malaise. Episodes of TD usually begin abruptly, occur during travel or soon after returning home, and are generally self-limited. The most important determinant of risk is the destination of the traveler. Attack rates of 20% to 50% are commonly reported. High-risk destinations include most of the developing countries of Latin America, Africa, the Middle East, and Asia. Intermediate-risk destinations include most of the southern European countries and a few Caribbean islands. Low-risk destinations include Canada, northern Europe, Australia, New Zealand, the United States, and some of the Caribbean islands.

TD is slightly more common in young adults than in older people. The reasons for this difference are unclear, but could include a lack of acquired immunity, more adventurous travel styles, and different eating habits. Attack rates are similar in men and women. The onset of TD is usually within the first week of travel, but can occur at any time during the visit and even after returning home.

TD is acquired through ingestion of fecally contaminated food or water, or both. Both cooked and uncooked foods might be implicated if they have been improperly handled. Especially risky foods include raw or undercooked meat and seafood and raw fruits and vegetables. Tap water, ice, and unpasteurized milk and dairy products can be associated with increased risk of TD; safe beverages include bottled carbonated beverages (especially flavored beverages), beer, wine, hot coffee or tea, or water boiled and appropriately treated with iodine or chlorine.

The place food is prepared appears to be an important variable, with private homes, restaurants, and street vendors listed in order of increasing risk.

TD typically results in four to five loose or watery stools per day. The median duration of diarrhea is 3 to 4 days. Approximately 10% of the cases persist longer than 1 week, approximately 2% longer than 1 month, and <1% longer than 3 months. Persistent diarrhea is, thus, quite uncommon and can differ considerably from acute TD with respect to etiology and risk factors. Approximately 15% of ill people experience vomiting, and 2% to 10% have diarrhea accompanied by fever or bloody stools, or both. Travelers can experience more than one episode of TD during a single trip. Rarely is TD life threatening.

Etiology

Infectious agents are the primary cause of TD. Travelers from developed countries to developing countries frequently experience a rapid, dramatic change in the type of organisms in their gastrointestinal tract. These new organisms often include potential enteric pathogens. Those who develop diarrhea have ingested an inoculum of virulent organisms sufficiently large to overcome individual defense mechanisms, resulting in symptoms.

Enteric Bacterial Pathogens

Enterotoxigenic *Escherichia coli* (ETEC) are among the most common causative agents of TD in all countries where surveys have been conducted. ETEC produce a watery diarrhea associated with cramps and a low-grade or no fever.

Salmonella gastroenteritis is a well-known disease that occurs throughout the world. In developed nations, this large group of organisms is the most common cause of outbreaks of food-associated diarrhea. In developing countries, the proportion of cases of TD caused by nontyphoidal salmonellae varies, but is not high. Salmonellae also can cause dysentery characterized by small-volume stools containing bloody mucus.

Shigellae are well known as the cause of bacillary dysentery. The shigellae are the cause of TD in up to 20% of travelers to developing countries.

Campylobacter jejuni is a common cause of diarrhea throughout the world; it is responsible for a small percentage of the reported cases of TD, some with bloody diarrhea. Additional studies are needed to determine how frequently it causes TD.

Vibrio parahaemolyticus is associated with ingestion of raw or poorly cooked seafood and has caused TD in passengers on Caribbean cruise ships and in people traveling in Asia. How frequently it causes disease in other areas of the world is unknown.

Less common bacterial pathogens include other diarrheagenic *E. coli*, *Yersinia enterocolitica*, *Vibrio cholerae* O1 and O139, non-O1 *V. cholerae*, *Vibrio fluvialis*, and possibly *Aeromonas hydrophila* and *Plesiomonas shigelloides*.

Viral Enteric Pathogens—Rotaviruses and Norwalk-like Virus

Along with the newly acquired bacteria, the traveler can also acquire many viruses. In six studies, for example, as much as 36% of diarrheal illnesses in travelers (median 22%) was associated with rotaviruses in the stools. However, a comparable number of asymptomatic travelers also had rotaviruses, and up to 50% of symptomatic people with rotavirus infections also had nonviral pathogens. Approximately 10% to 15% of travelers develop serologic evidence of infection with Norwalk-like viruses. The roles of adenoviruses, astroviruses, coronaviruses, enteroviruses, or other viral agents in causing TD are even less clear. Although viruses are commonly acquired by travelers, they do not appear to be frequent causes of TD in adults.

Parasitic Enteric Pathogens

While less commonly implicated as the cause of TD than bacteria, enteric protozoa are recognized etiologic agents of TD. In the small number of studies that have included appropriate testing for these parasites in travelers or expatriates in developing countries, a variable proportion of TD has been attributed to *Giardia intestinalis* (0% to 12%), *Entamoeba histolytica* (0% to 5%), *Cryptosporidium parvum* (2% to 5%), and *Cyclospora cayetanensis* (1% to 11%). The likelihood of a parasitic etiology is higher when diarrheal illness is prolonged. *E. histolytica* should be considered when the patient has dysentery or invasive diarrhea (bloody stools). Specific diagnostic testing is required to identify *E. histolytica*, *C. parvum*, and *C. cayetanensis*. *Dientamoeba fragilis*, *Isospora belli*, *Balantidium coli*, and *Strongyloides stercoralis* can cause occasional cases of TD. While not common causes of TD, these parasites should be considered in persistent, unexplained cases.

Unknown Causes

No data have been presented to support noninfectious causes of TD, such as changes in diet, jet lag, altitude, and fatigue. Existing evidence indicates that in all but a few instances, such as drug-induced or preexisting gastrointestinal disorders, an infectious agent or agents can cause diarrhea in travelers. However, even with the application of the best existing methods for detecting bacteria, viruses, and parasites, 20% to 50% of cases of TD remain without recognized etiologies.

Prevention

There are four possible approaches to prevention of TD: (1) instruction regarding food and beverage consumption, (2) immunization, (3) use of nonantimicrobial medications, and (4) use of prophylactic

antimicrobial drugs. Data indicate that meticulous attention to food and beverage consumption, as mentioned previously, can decrease the likelihood of developing TD. Most travelers, however, encounter difficulty in observing the requisite dietary restrictions.

No available vaccines and none that are expected to be available in the next 3 years are effective against TD. Several nonantimicrobial agents have been advocated for prevention of TD. Available controlled studies indicate that prophylactic use of difenoxine, the active metabolite of diphenoxylate (Lomotil®), actually increases the incidence of TD, in addition to producing other undesirable side effects. Antiperistaltic agents (for example, Lomotil® and Imodium®) are not effective in preventing TD. No data support the prophylactic use of activated charcoal.

Bismuth subsalicylate, taken as the active ingredient of Pepto-Bismol® (2 ounces four times a day, or two tablets four times a day), has decreased the incidence of diarrhea by about 60% in several placebo-controlled studies. Side effects include temporary blackening of the tongue and stools; occasional nausea and constipation; and, rarely, tinnitus. Available data are not sufficient to exclude a risk to the traveler from the use of such large doses of bismuth subsalicylate for a period of more than 3 weeks. Bismuth subsalicylate should be avoided by travelers with aspirin allergy, renal insufficiency, and gout, and by those who are taking anticoagulants, probenecid, or methotrexate. In travelers already taking aspirin or related salicylates for arthritis, large concurrent doses of bismuth subsalicylate can produce toxic serum concentrations of salicylate. Caution should be used in giving bismuth subsalicylate to children and adolescents with chickenpox or influenza because of a potential risk of Reye's syndrome. Bismuth subsalicylate has not been approved for infants and children younger than 3 years of age. Bismuth subsalicylate appears to be an effective prophylactic agent for TD, but is not recommended for prophylaxis of TD for periods of more than 3 weeks. Further studies of the efficacy and side effects of lower dose regimens are needed.

Controlled data are available on the prophylactic value of several other nonantimicrobial drugs. Enterovioform® and related halogenated hydroxyquinoline derivatives (for example, clioquinol, iodoquinol, Mexaform®, and Intestopan®) are not helpful in preventing TD, can have serious neurologic side effects, and should never be used for prophylaxis of TD.

Controlled studies have indicated that a variety of antibiotics, including doxycycline, trimethoprim/sulfamethoxazole (TMP/SMX), trimethoprim alone, and the fluoroquinolone agents ciprofloxacin and norfloxacin, when taken prophylactically have been 52% to 95% effective in preventing TD in several areas of the developing world. The effectiveness of these agents, however, depends on the antibiotic resistance patterns of the pathogenic bacteria in each area of travel, and such information is seldom available. Resistance to fluoroquinolones is the least common, but this is changing as use of these agents increases worldwide.

Although effective in preventing some bacterial causes of diarrhea, antibiotics have no effect on the acquisition of various viral and parasitic diseases. Prophylactic antibiotics can give travelers a false sense of security about the risk associated with consuming certain local foods and beverages.

The benefits of widespread prophylactic use of doxycyline, fluroquinolones, TMP/SMX, or TMP alone in several million travelers must be weighed against the potential drawbacks. The known risks include allergic and other side effects (such as common skin rashes, photosensitivity of the skin, blood disorders, Stevens-Johnson syndrome, and staining of the teeth in children), as well as other infections that might be induced by antimicrobial therapy (such as antibiotic-associated colitis, *Candida* vaginitis, and *Salmonella* enteritis). Because of the uncertain risk involved in the widespread administration of these antimicrobial agents, their prophylactic use is not recommended. Although it seems reasonable to use prophylactic antibiotics in certain high-risk groups, such as travelers with immunosuppression or immunodeficiency, no data directly support this practice. There is little evidence that other disease entities are worsened sufficiently by an episode of TD to risk the rare undesirable side effects of prophylactic antimicrobial drugs. **Therefore, prophylactic antimicrobial agents are not recommended for travelers.** Instead, available data support the recommendation that travelers be instructed in sensible dietary practices as a prophylactic measure. This recommendation is justified by the excellent results of early treatment of TD as outlined in the following section. Some travelers might wish to consult with their physicians and might elect to use prophylactic antimicrobial agents for travel under special circumstances, once the risks and benefits are clearly understood.

Treatment

Travelers with TD have two major complaints for which they desire relief—abdominal cramps and diarrhea. Many agents have been proposed to control these symptoms, but few have been demonstrated to be effective in rigorous clinical trials.

Nonspecific Agents

A variety of "adsorbents" have been used in treating diarrhea. For example, activated charcoal has been found to be ineffective in the treatment of diarrhea. Kaolin and pectin have been widely used for diarrhea. While the combination appears to give the stools more consistency, it has not been shown to decrease cramps and frequency of stools or to shorten the course of infectious diarrhea. Lactobacillus preparations and yogurt have also been advocated, but no evidence supports use of these treatments for TD.

Bismuth subsalicylate preparation (1 ounce of liquid or two 262.5-milligram [mg] tablets every 30 minutes for eight doses) decreased the frequency of stools and shortened the duration of illness in several placebo-controlled studies. Treatment was limited to 48 hours at most, with no more than eight doses in a 24-hour period. There is concern about taking large amounts of bismuth and salicylate without supervision, especially for people who might be intolerant of salicylates, who have renal insufficiency, or who take salicylates for other reasons.

Antimotility Agents

Antimotility agents are widely used in treating diarrhea of all types. Natural opiates (paregoric, tincture of opium, and codeine) have long been used to control diarrhea and cramps. Synthetic agents, such as diphenoxylate and loperamide, come in convenient dosage forms and provide prompt symptomatic

but temporary relief of uncomplicated TD. However, they should not be used by people with high fever or with blood in the stools. Use of these drugs should be discontinued if symptoms persist beyond 48 hours. Diphenoxylate and loperamide should not be used in infants younger than 2 years of age.

Antimicrobial Treatment

Travelers who develop diarrhea with three or more loose stools in an 8-hour period, especially if associated with nausea, vomiting, abdominal cramps, fever, or blood in the stools, might benefit from antimicrobial treatment. A typical 3- to 5-day illness can often be shortened to 1 to 1 1/2 days by effective antimicrobial agents. The effectiveness of antibiotic therapy will depend on the etiologic agent and its antibiotic sensitivity. The antibiotic regimen most likely to be effective is ciprofloxacin (500 mg) taken twice a day. Other fluroquinolones, such as norfloxacin, ofloxacin, or levofloxacin might be equally as effective. Fewer side effects and less widespread antibiotic resistance has been reported with the fluoroquinolones than with TMP/SMX. Three days of treatment is recommended, although 2 or fewer days might be sufficient. Nausea and vomiting without diarrhea should not be treated with antimicrobial drugs.

Travelers should be advised to consult a physician rather than attempt self-medication if the diarrhea is severe or does not resolve within several days; if there is blood or mucus, or both, in the stools; if fever occurs with shaking chills; or if there is dehydration with persistent diarrhea.

Oral Fluids

Most cases of diarrhea are self-limited and require only simple replacement of fluids and salts lost in diarrheal stools. This is best achieved by use of an oral rehydration solution such as World Health Organization oral rehydration salts (ORS) solution (Table 4-2). This solution is appropriate for treating as well as preventing dehydration. Travelers should be advised that ORS packets are available at stores or pharmacies in almost all developing countries. ORS is prepared by adding one packet to boiled or treated water. Packet instructions should be checked carefully to ensure that the salts are added to the correct volume of water. ORS solution should be consumed or discarded within 12 hours if held at room temperature or 24 hours if kept refrigerated.

Travelers should be advised to avoid iced drinks and noncarbonated bottled fluids made from water of uncertain quality. Dairy products aggravate diarrhea in some people and travelers with diarrhea should be advised to avoid them.

Infants With Diarrhea

Infants 2 years of age or younger are at high risk of acquiring TD. The greatest risk to the infant with diarrhea is dehydration (Table 4-3). Travelers should be advised that dehydration is best prevented by use of the WHO ORS solution in addition to the infant's usual food. ORS packets are available at stores or pharmacies in almost all developing countries. ORS is prepared by adding one packet to boiled or treated water. Travelers should be advised to check packet instructions carefully to ensure

Table 4-2.—Composition of World Health Organization Oral Rehydration Solution (ORS) for Diarrheal Illness.

INGREDIENT	AMOUNT
Sodium chloride	3.5 grams per liter
Potassium chloride	1.5 grams per liter
Glucose	20.0 grams per liter
Trisodium citrate*	2.9 grams per liter

*An earlier formulation that used sodium bicarbonate 2.5 grams per liter had a shorter shelf-life, but was physiologically equivalent and might still be produced in some countries.

that the salts are added to the correct volume of water. ORS solution should be consumed or discarded within 12 hours if held at room temperature, or 24 hours if kept refrigerated. A dehydrated child will drink ORS avidly; travelers should be advised to give it to the child as long as the dehydration persists. An infant who vomits the ORS will usually keep it down if it is offered by spoon in frequent small sips. Breast-fed infants should continue nursing on demand. For bottle-fed infants, full-strength, lactose-free or lactose-reduced formulas should be administered. Older infants and children receiving semi-solid or solid foods should continue to receive their usual diet during the illness. Recommended foods include starches, cereals, yogurt, fruits, and vegetables. Immediate medical attention is required for the infant with diarrhea who develops signs of moderate to severe dehydration (Table 4-3), bloody diarrhea, >30° Celsius (>102°Fahrenheit) fever, or persistent vomiting. While medical attention is being obtained, the infant should be offered ORS.

More information is available from the CDC in a publication entitled, "The Management of Acute Diarrhea in Children: Oral Rehydration, Maintenance, and Nutritional Therapy" (MMWR No. RR-16, October 16, 1992). ORS packets are available in the United States from Jianas Brothers Packaging Company, 2533 Southwest Boulevard, Kansas City, Missouri 64108 (1-816-421-2880). Also, Cera Products, 8265 I Patuxent Range Road, Jessup, Maryland 20794 (1-410-997-2334 or 1-888-Ceralyte), markets a cereal- rather than a glucose-based product, Ceralyte, in several different flavors.

Precautions for Children and Pregnant Women

Although infants and children do not make up a large proportion of travelers to high-risk areas, some children do accompany their families. Teenagers should follow the advice given to adults, with possible adjustments of doses of medication. Physicians should be aware of the risks of tetracyclines for infants and children younger than 8 years of age. Few data are available about the usage of antidiarrheal drugs in infants and children. Drugs should be prescribed with caution for pregnant women and nursing mothers.

Table 4-3.—Assessment of Dehydration Levels in Infants.

SIGNS	SEVERITY		
	Mild	**Moderate**	**Severe**
General Condition	Thirsty, restless, agitated	Thirsty, restless, irritable	Withdrawn, somnolent, or comatose
Pulse	Normal	Rapid, weak	Rapid, weak
Anterior fontanelle	Normal	Sunken	Very sunken
Eyes	Normal	Sunken	Very sunken
Tears	Present	Absent	Absent
Urine	Normal	Reduced, concentrated	None for several hours
Weight loss	4% to 5%	6% to 9%	10% or more

CRUISE SHIP TRAVEL

Preventive Measures

International cruise ship travelers often are uncertain about the vaccines and prevention behaviors applicable to their particular cruise itineraries. Cruise ships often visit international ports and passengers disembark to sightsee and to experience the local culture; however, among cruise ship passengers, risk of exposure to geographic-specific infectious diseases is difficult to quantify because of limited data. Because of this difficulty, the Centers for Disease Control and Prevention (CDC) recommends following those prevention and vaccine recommendations that apply to each country visited (as detailed in this text and at CDC's Travelers Health website at http://www.cdc.gov/travel). The traveler should be advised to consult with a travel health advisor or a primary health care provider who may chose to modify the recommendations depending on the length of the traveler's visit ashore.

Sanitation

In 1975, because of several major disease outbreaks on cruise vessels, the Centers for Disease Control and Prevention (CDC) established the Vessel Sanitation Program (VSP) as a cooperative activity with the cruise ship industry. This joint program strives to achieve and maintain a level of sanitation on

passenger vessels that will lower the risk of gastrointestinal disease outbreaks and provide a healthful environment for passengers and crews. CDC addresses the program goals by encouraging the industry to establish and maintain a comprehensive sanitation program and overseeing of its success through an inspection process. Every vessel having a foreign itinerary and carrying 13 or more passengers is subject to twice yearly unannounced inspections and, when necessary, reinspections. Inspections, conducted only at ports under U.S. control, cover such environmental aspects as:

1. Water supply, storage, distribution, backflow protection, and disinfection.

2. Food handling during storage, preparation, and service, and product temperature control.

3. Potential contamination of food, water, and ice.

4. Employee practices and personal hygiene.

5. General cleanliness, facility repair, and vector control.

6. Training programs in general environmental and public health practices.

A score of 86 or higher at the time of the inspection indicates that the ship is providing an acceptable standard of sanitation. In general, the lower the score, the lower the level of sanitation; however, a low score does not necessarily imply an imminent risk of an outbreak of gastrointestinal disease or other illness related to environmental sanitation. Each ship is required to document a plan for corrective action following each inspection. Inspectors will recommend a ship not sail if they detect an imminent health hazard aboard ship (for example, inadequate facilities for maintaining safe food temperatures or a contaminated drinking water system). Full information on inspection criteria can be obtained by writing to the VSP office at the address listed at the end of this section. At any time, the Director of CDC may determine that failure to implement corrective actions presents a threat of communicable disease being introduced into the United States and may take additional action, including detaining the ship in port.

The scores and inspection reports for each ship are available via the Internet at http://www.cdc.gov/nceh/vsp. Scores are also published biweekly in the *Summary of Sanitation Inspections of International Cruise Ships*, commonly known as the "Green Sheet." This sheet is distributed to travel-related services worldwide and is a way to communicate a ship's compliance with VSP recommendations both to the cruise ship industry and to the consumer. The Green Sheet is also available via the Internet site, as well as the CDC fax information service (1-888-232-6789; request information on "Cruise Ship Sanitation Inspection Updates"). Information can also be requested by sending an e-mail to vsp@cdc.gov or by writing to the Vessel Sanitation Program, National Center for Environmental Health, CDC, 4770 Buford Highway, NE, Mailstop F-16, Atlanta, Georgia 30341-3724.

SPRAYING AIRCRAFT FOR INSECTS—DISINSECTION

International travelers should be advised that some countries require the spraying of the aircraft passenger compartment with insecticide while passengers are present. This practice is called disinsection, and is used to prevent the importation of insects such as mosquitoes. While these recommended disinsection procedures have been determined to be safe by the World Health Organization, they can aggravate certain health conditions (for example, allergies). Countries that might spray the passenger cabin for insects are located in Latin America, the Caribbean, Australia, and the South Pacific region.

Travelers who are interested in determining what disinsection procedures might be performed on a particular flight should be advised to see the U.S. Department of Transportation web site at http://www.ostpxweb.dot.gov/policy/safety/disin.htm.

ENVIRONMENTAL EFFECTS

International travelers can be subject to certain stresses that can lower resistance to disease, such as crowding; disruption of usual eating and drinking habits; and time changes, with "jet lag" contributing to a disturbed pattern of the sleep and wakefulness cycle. These conditions of stress can lead to nausea, indigestion, fatigue, or insomnia. Complete adaptation depends on the number of time zones crossed and can take a week or more.

Heat and cold can be directly or indirectly responsible for some diseases and can give rise to serious skin conditions. Dermatophytoses such as athlete's foot are often made worse by warm, humid conditions.

Excessive heat and humidity alone, or strenuous activity under those conditions, can lead to heat exhaustion from salt and water deficiency and to the more serious heat stroke or hyperthermia. Travelers who anticipate being exposed to excessive heat should be advised to increase consumption of nonalcoholic liquids and to be aware of signs of heat illness, such as headache; dizziness; and red, hot, and dry skin. The ultraviolet rays of the sun can cause severe and very debilitating sunburn in lighter skinned people. Wearing a wide-brimmed hat and using a sun screen with a sun protection factor (SPF) of 15 or higher on exposed skin will reduce the likelihood of severe sunburn.

Excessive cold affects people who might be inadequately dressed or who remain outside for extended periods of time. Cold particularly affects the elderly and the young. Exposure to cold can lead to hypothermia and to frostbite of exposed parts of the body. Alcohol consumption can amplify the adverse effects of cold temperatures.

Breathing and swallowing dust when traveling on unpaved roads or in arid areas can be followed by nausea and malaise and can cause increased susceptibility to infections of the upper respiratory tract. The harmful effects of air pollution are difficult to avoid when visiting some cities; limiting strenuous activity and not smoking can help.

ALTITUDE ILLNESS

Travelers whose itineraries will take them above an altitude of 1,829 to 2,438 meters (6,000 to 8,000 feet) should be aware of the risk of altitude illness. Travelers are exposed to higher altitudes in a number of ways: by mountain climbing or trekking in or to high-altitude destinations such as Cusco, Peru (3,000 meters [11,000 feet]); La Paz, Bolivia (3,444 meters [11,300 feet]); or Lhasa, Tibet (3,749 meters [12,500 feet]). Travelers with underlying medical conditions, such as congestive heart failure or pulmonary insufficiency, should be advised to consult a doctor familiar with high-altitude illness before undertaking such travel. The risk of ischemic heart disease does not appear to be increased at high altitudes, but having a heart attack in a remote area increases the problems of obtaining appropriate treatment.

Travelers vary considerably in their susceptibility to altitude illness, and there are currently no screening tests that predict whether someone is at greater risk of getting altitude illness. Past experience is the most reliable guide; susceptibility to altitude illness appears to be genetic, and is not affected by training or physical fitness.

Altitude illness is divided into three syndromes: acute mountain sickness (AMS), high-altitude cerebral edema (HACE), and high-altitude pulmonary edema (HAPE). AMS is the most common presentation of altitude illness and, while it can occur at altitudes as low as 1,219 to 1,829 meters (4,000 to 6,000 feet), most often occurs in abrupt ascents to over 2,743 meters (9,000 feet). The symptoms resemble an alcohol hangover: headache; profound fatigue; loss of appetite; nausea; and, occasionally, vomiting. The onset of AMS is delayed, usually beginning at least 6 to 12 hours after arrival at a higher altitude.

HACE is considered a severe progression of AMS. In addition to the AMS symptoms, lethargy becomes profound, confusion can manifest, and ataxia will be demonstrated during the tandem gait test. The tandem gait test—having the traveler walk a straight line while placing the heel of the front foot against the toe of the rear foot—is the best test for determining whether HACE is present. A traveler who falls off the line while trying to do the tandem gait test has HACE by definition, and immediate descent is mandatory.

HAPE can occur by itself or in conjunction with HACE. The initial symptoms are increased breathlessness with exertion, and eventually increased breathlessness at rest. The diagnosis can usually be made when breathlessness fails to resolve after several minutes of rest. At this point, it is critical to descend to a lower altitude.

The main point of instructing travelers about altitude illness is not to prevent any possibility of getting altitude illness, but to prevent deaths from altitude illness. The onset of symptoms and clinical course are slow enough and predictable enough that there is no reason for someone to die from altitude illness unless trapped by weather or geography in a situation in which descent is impossible. The three rules that travelers should be made aware of to prevent death from altitude illness are:

1. Learn the early symptoms of altitude illness and recognize when personally suffering from them.

2. Never ascend to sleep at a higher altitude when experiencing any of the symptoms of altitude illness.
3. Descend if the symptoms become worse while resting at the same altitude.

Studies have shown that travelers who are on organized group treks to high-altitude locations are more likely to die of altitude illness than travelers who are by themselves. This is most likely the result of group pressure (whether perceived or real) and a fixed itinerary. The most important aspect of preventing severe altitude illness is to refrain from further ascent until all symptoms of altitude illness have disappeared.

Children are as susceptible to altitude illness as adults, and young children who cannot talk can show very nonspecific symptoms, such as loss of appetite and irritability. There are no studies or case reports of harm occurring to a fetus if the mother travels briefly to a high altitude during pregnancy. However, most authorities recommend that pregnant women stay below 3,658 meters (12,000 feet) if possible.

Three medications have been shown to be useful in the prevention and treatment of altitude illness. Acetazolamide (Diamox®) can prevent AMS when taken prior to ascent, and can speed recovery if taken after symptoms have developed. The drug appears to work by acidifying the blood, which causes an increase in respiration and thus aids in acclimatization. The standard dose is 250 milligrams (mg) BID (*bis in die*, that is, "twice daily"), usually starting the day prior to ascent. Anecdotal observations support the use of 125 mg BID as being equally effective with fewer side effects. Allergic reactions to acetazolamide are extremely rare, but the drug is related to sulfonamides, and should not be used by sulfa-allergic travelers.

Dexamethasone has been shown to be effective in the prevention and treatment of AMS and HACE. The drug prevents symptoms, but there is no evidence that it aids acclimatization. Thus, there is a risk of a sudden of symptoms if the traveler goes off the drug while ascending. It is preferable for the traveler to use acetazolamide to prevent AMS while ascending, and to reserve the use of dexamethasone to treat severe symptoms. The dosage is 4 mg every 6 hours.

Nifedipine has been shown to prevent and ameliorate HAPE in people who are particularly susceptible to HAPE. The dosage is 10 mg every 8 hours.

For the majority of travelers, the best way to avoid altitude illness is to plan a gradual ascent. If this is not possible, acetazolamide may be used prophylactically, and dexamethasone and nifedipine may be carried for emergencies.

NATURAL DISASTERS AND ENVIRONMENTAL HAZARDS

Natural disasters can contribute to the transmission of some diseases; however, unless the causative agent is in the environment, transmission cannot take place. Natural disasters often disrupt water

supplies and sewage systems. Epidemic typhoid has been conspicuously absent following natural disasters in developing countries where typhoid is endemic. It takes several weeks for typhoid antibodies to develop, and even then immunization provides only moderate protection. Floods pose no additional risk of typhoid. In flood areas where the organism has been present, recent studies have identified outbreaks of leptospirosis. (See Chapter 3, "Specific Recommendations for Vaccinations and Disease Prevention," "Leptospirosis," pages 104 and 105, for information on how to minimize the risk of infection.)

Of greatest important in preventing enteric disease transmission when water and sewage systems have been disrupted is ensuring that water and food supplies are safe to consume. If contamination is suspected, water should be boiled and appropriately disinfected. (See "Risks From Food and Drink," "Water," this section, pages 165 and 166).

Contamination of rivers and lakes with chemical or organic or inorganic compounds (such as heavy metals or other toxins) can be harmful both to fish and to the humans who eat the fish or who swim or bathe in the water. Sufficient warning that such a hazard exists in a body of water is often difficult to provide.

Air pollution is widespread in large cities. Uncontrolled forest fires have been known to cause widespread pollution over vast expanses of the world. Health risks associated with these environmental occurrences have not been fully studied, and travelers with chronic pulmonary disease might be more susceptible to respiratory infection. Any risk to short-term healthy travelers to such areas is probably small.

CHERNOBYL

Effects of the Radiological Release at Chernobyl

The Chernobyl nuclear power station, located in Ukraine about 100 kilometers (62 miles) northwest of Kiev, Ukraine, and 310 kilometers (km) (193 miles) southeast of Minsk, Belarus, had an uncontrolled release of radioactive material in April 1986. This event resulted in the largest short-term release of radioactive materials into the atmosphere ever recorded. The radiologic contamination primarily affected three republics: Ukraine, Belarus, and Russia. The highest radioactive ground contamination occurred within 30 km (19 miles) of Chernobyl. The level of contamination in any given area is decreasing with the passage of time, but it will be many years before levels of radioactivity in some parts of these countries return to the levels that existed prior to the Chernobyl event.

Area Considerations

Short-term international travelers (those who plan to stay in the region less than a few months) to Ukraine, Belarus, and Russia should not be concerned about residing in areas that are not controlled (marked with signs or fenced). However, long-term travelers should be advised that, in some

uncontrolled areas, they could receive a radiation dose from the radioactive ground contamination in excess of the international radiological health standards recommended for the public. Long-term travelers should investigate local conditions prior to choosing a long-term residence. (For example, ground contamination that exceeds 5 curies per square kilometer [5 Ci/km^2] of cesium-137 could result in a radiation dose greater than the recommended standards.) Staff of the appropriate U.S. embassy should be able to assist in this investigation.

Food and Water Considerations

Officials of the three republics attempt to monitor all foodstuffs sold in the public markets for levels of radioactivity. Radioactive concentration limits have been established for various classes of food (for example, milk, meat, and vegetables). These limits are comparable with standards used by many western nations, including the European Union. Foods with contamination levels in excess of these limits are not allowed to be sold in the markets. Private farmers regularly make foods available for sale outside the official market system. These foods are not monitored for radioactivity, and travelers should not consume them. Likewise, travelers should be advised not eat any wild berries, wild mushrooms, or wild game from these regions and should drink only bottled water.

Age and Health Considerations

Young children, unborn babies, and nursing infants are potentially at greater risk from exposure to radiation than adults. Pregnant or nursing mothers should be advised to pay extra attention to acquiring food from reliable, well-monitored sources.

INJURIES

Injuries, especially those from motor vehicle crashes, pose a great risk of serious disability or loss of life to international travelers. The risk of motor vehicle-related death is generally many times higher in developing countries than in the United States. Motor vehicle crashes result from a variety of factors, including inadequate roadway design, hazardous conditions, lack of appropriate vehicles and vehicle maintenance, unskilled or inexperienced drivers, inattention to pedestrians and cyclists, or impairment due to alcohol or drug use; all these factors are preventable or can be abated. Defensive driving is an important preventive measure. When driving or riding, travelers should be advised to request a vehicle equipped with safety belts and, where available, to use them. Travelers should carefully inspect vehicles to ensure that tires, windshield wipers, and brakes are in good condition and that all lights are in good working order. Travelers should also request a vehicle equipped with air bags, where available. Because a high proportion of crashes occur at night when drivers are returning from social events, travelers should avoid nonessential night driving, alcohol, and riding with people who are under the influence of alcohol or drugs. Night driving outside urban areas in developing countries is particularly risky. The risk of death in a motor vehicle crash is greater for people sitting in the front seat than for those in the rear seat. Travelers should ride in the rear seats of motor vehicles, where possible. In addition, travelers should be strongly urged to be familiar with local

recommendations about what to do if their vehicle is involved in a crash, especially one involving injuries. Such situations can quickly become dangerous for drivers and passengers.

Pedestrian, bicycle, and motorcycle travel are often dangerous as well, and helmet use is imperative for bicycle and motorcycle travel. In developing countries where helmets will likely not be available, travelers should be advised to bring their own with them if they plan to ride bicycles or motorcycles. Travelers with young children should be advised to bring their own child safety seats.

Fire injuries are also a significant cause of injuries and death. Travelers should be reminded not to smoke in bed, and to inquire about whether hotels have smoke detectors and sprinkler systems. Travelers might wish to bring their own smoke detectors with them. Travelers should always locate primary and alternate escape routes from rooms in which they are meeting or staying. Travelers should also be advised to look for improperly vented heating devices that might cause carbon monoxide poisoning. Travelers should be reminded to escape a fire by crawling low under smoke.

Other major causes of injury trauma include drowning (see "Swimming Precautions," this chapter, page 183) and injuries to water skiers and divers from boat propellers. Travelers should use boats equipped with propeller guards whenever possible, and wear a personal flotation device (life jacket) whenever riding in a boat.

Travelers should also be aware of the potential for violence-related injuries. Risk for assault or terrorist attack varies from country to country; travelers should heed advice from residents and tour guides about areas to be avoided, going out at night, and going out alone. Travelers should be advised not to fight attackers and, if confronted, to give up their valuables. For more information, travelers may be advised to contact the U.S. Department of State, Overseas Citizens Emergency Center at 1-202-647-5225 or the website, http://www.travel.state.gov, for specific country travel warnings and information.

ANIMAL-ASSOCIATED HAZARDS

Animals in general tend to avoid human beings, but they can attack, particularly if they are protecting their young or territory. Travelers should be reminded that, in areas of endemic rabies, domestic dogs, cats, or other animals should not be petted, handled, or fed. Wild animals should be avoided; most injuries from wild animals are the direct result of attempting to pet, handle, or feed the animals.

The bites and stings of and contact with some insects cause unpleasant reactions. Travelers should be advised to seek medical attention if an insect bite or sting causes redness, swelling, bruising, or persistent pain. Many insects also transmit communicable diseases. Some insects can bite and transmit disease without the traveler's being aware of the bite, particularly when the traveler is camping or staying in rustic or primitive accommodations. Travelers should be advised to use insect repellents, protective clothing, and mosquito netting when visiting many parts of the world. (See "Protection Against Mosquitoes and Other Arthropod Vectors," this chapter, pages 163 through 165.)

Poisonous snakes are hazards in many locations, although deaths from snake bites are relatively rare. The Australian brown snake, Russell's viper and cobras in southern Asia, carpet vipers in the Middle East, and coral snakes and rattlesnakes in the Americas are particularly dangerous. Most snake bites are the direct result of handling or harassing snakes, which bite as a defensive reaction. Attempts to kill snakes are dangerous, often leading to bites on the fingers. The venom of a small or immature snake can be even more concentrated than that of larger ones; therefore, all snakes should be left alone.

Fewer than half of all snake bite wounds actually contain venom, but travelers should be advised to seek medical attention any time a bite wound breaks the skin. A pressure bandage, ice (if available), and immobilization of the affected limb are recommended first-aid measures while the victim is moved as quickly as possible to a medical facility. Specific therapy for snake bite is controversial, and should be left to the judgment of local emergency medical personnel. Snakes tend to be active at night and in warm weather. As a precaution, boots and long pants should be worn when walking outdoors at night in snake-infested regions. Bites from scorpions can be painful, but seldom are dangerous, except possibly in infants. In general, exposure to bites can be avoided by sleeping under mosquito nets and by shaking clothing and shoes before putting them on, particularly in the morning. Snakes and scorpions tend to rest in shoes and clothing.

SWIMMING PRECAUTIONS

Swimming in contaminated water can result in skin, eye, ear, and certain intestinal infections, particularly if the swimmer's head is submerged. Generally, for infectious disease prevention, only pools that contain chlorinated water can be considered safe places to swim. In certain areas, fatal primary amebic meningoencephalitis has occurred following swimming in warm, dirty water. Travelers who swim should be advised to avoid beaches that might be contaminated with human sewage or with dog feces. Travelers should also be advised to avoid wading or swimming in freshwater streams, canals, and lakes that are likely to be infested with the snail hosts of schistosomiasis (bilharziasis) or contaminated with urine from animals infected with Leptospira. Biting and stinging fish, corals, and jelly fish can also be hazardous.

Travelers should be advised never to swim alone or when under the influence of alcohol or drugs. Likewise, they should never dive or jump into an unfamiliar body of water without first determining the depth (at least 9 feet for jumping and diving) and the terrain, and whether there are any hidden obstacles. Travelers should be advised to learn cardiopulmonary resuscitation (CPR) and basic first-aid. They should be aware of the weather conditions and forecasts. Thunderstorms or even strong winds are dangerous for swimmers and boaters. They should use a personal flotation device (life jacket) when boating, skiing, or using personal water craft regardless of the distance to be traveled, the size of the boat, or their swimming ability. Travelers should be cautioned to remember that open water usually has limited visibility, and conditions can sometimes change from hour to hour. Currents are often unpredictable, moving rapidly and quickly changing direction. A strong water current can carry even expert swimmers far from shore.

RECREATIONAL WATER

A variety of infections (such as skin, ear, respiratory, and diarrheal infections) have been linked to wading or swimming in the ocean, freshwater lakes and rivers, and swimming pools. The water can be contaminated by other people, and from sewage, animal wastes, and waste water runoff.

Diarrhea can be spread when disease-causing germs from human or animal feces are introduced into the water. Accidentally swallowing small amounts of fecally contaminated water can then cause disease. Travelers should be warned to avoid swallowing water while engaging in aquatic activities. Some organisms (*Cryptosporidium, Giardia,* hepatitis A, and Norwalk virus) have moderate to very high resistance to chlorine levels commonly found in chlorinated swimming pools, so travelers also should avoid swallowing chlorinated swimming pool water.

Travelers should be advised to avoid swimming or wading with open cuts or abrasions that might serve as entry points for germs and to protect nasal membranes from germs by wearing nose plugs when entering untreated water venues. They should also avoid freshwater in schistosomiasis-endemic areas of the Caribbean, South America, Africa, and Asia (see Chapter 3, "Specific Recommendations for Vaccinations and Disease Prevention," "Schistosomiasis," pages 141 and 142 for further precautions).

EMERGING INFECTIOUS DISEASES

Emerging infectious disease are diseases of infectious origin whose incidence in humans has increased within the past two decades or threatens to increase in the near future. Many factors, or combinations of factors, can contribute to disease emergence. New infectious diseases can emerge from genetic changes in existing organisms; known diseases can spread to new geographic areas and populations; and previously unknown diseases can appear in humans living or working in changing ecologic conditions that increase their exposure to insect vectors, animal reservoirs, or environmental sources of novel pathogens. Reemergence can occur because of the development of antimicrobial resistance in existing infections (for example, gonorrhea, malaria, and pneumococcal disease) or breakdowns in public health measures for previously controlled infections (for instance, cholera, tuberculosis, and pertussis). For current outbreak bulletins on diseases of international concern, travelers should be advised to call the Centers for Disease Control and Prevention Travelers' Health hotline at 1-877-FYI-TRIP (1-877-394-8747).

ILLNESS ABROAD

If Medical Care Is Needed Abroad

If an American citizen becomes seriously ill or is injured abroad, a U.S. consular officer can assist in locating appropriate medical services and informing family or friends. If necessary, a consular

officer can also assist in the transfer of funds from the United States. However, the traveler should be advised that payment of hospital and other expenses is his or her personal responsibility. See the U.S. Department of State website at http://www.travel.state.gov/acs.html#medical.

Protection against potentially hazardous drugs is nonexistent in some countries, increasing the risk of adverse reactions. Travelers should be advised not to buy medications "over the counter" unless they are familiar with the products.

Before going abroad, travelers should be advised to learn what medical services their health insurance will cover overseas. If the health insurance policy provides coverage outside the United States, travelers should be advised to carry both the insurance policy identity card (as proof of insurance) and a claim form. Although some health insurance companies will pay "customary and reasonable" hospital costs abroad, very few will pay for medical evacuation to the United States. Medical evacuation can easily cost $10,000 or more, depending on the location and medical condition.

World Health Organization (WHO) Blood Transfusion Guidelines for International Travelers

There is a growing public awareness of the acquired immunodeficiency syndrome (AIDS) epidemic and a resulting concern about acquiring human immunodeficiency virus (HIV) through blood transfusion. Accurate and systematic screening of all blood donations is not yet feasible in all developing countries. Travelers planning international itineraries have requested to have their own blood or blood from their home country available to them in case of urgent need. These requests raise logistical, technical, and ethical issues that are not easy to resolve. Ultimately, the safety of blood for such travelers will depend on the quality of blood transfusion services in the host country. The strengthening of these services is of the highest priority. While efforts are being made to achieve this end, other approaches are also needed.

Basic Principles

1. Unexpected, emergency blood transfusion is rarely required. It is needed only in situations of massive hemorrhage, such as severe trauma, gynecologic and obstetric emergency, or gastro-intestinal bleeding.

2. In many cases, resuscitation can be achieved by use of colloid or crystalloid plasma expanders instead of blood.

3. Blood transfusion is not free of risk, even in the best of conditions. In most developing countries, the risk is increased by limited technical resources for screening blood donors for HIV infection and other diseases transmissible by blood.

4. The international shipment of blood for transfusion is practical only when handled by agreement between two responsible organizations, such as national blood transfusion services. This

mechanism is not useful for the emergency needs of individual travelers and should not be attempted by private travelers or organizations not operating recognized blood programs.

Therefore, travelers should be made aware that:

1. There are no medical indications for travelers to take blood with them from their home countries.

2. The limited storage period of blood and the need for special equipment negate the feasibility of independent blood banking for individual travelers or small groups.

3. Blood should be transfused only when absolutely indicated. This applies even more forcefully in those countries where screening of blood for transmissible diseases is not yet widely performed.

Therefore, the following options should be recommended in emergency situations:

1. When urgent resuscitation is necessary, the use of plasma expanders rather than blood should always be considered.

2. In case of emergency need for blood, use of plasma expanders and urgent evacuation home might be the actions of choice.

3. When blood transfusion cannot be avoided, the attending physician should make every effort to ensure that the blood has been screened for transmissible diseases, including HIV.

4. International travelers should be advised to:

    a. Take active steps to minimize the risk of injury, such as avoiding night driving, employing safe driving practices, and wearing safety belts whenever possible.

    b. Establish a plan for dealing with medical emergencies.

    c. Support the development within countries of safe and adequate blood supplies.

This information is taken from the WHO publication "World Health Organization Global Programme on AIDS: Blood Transfusion Guidelines for International Travelers."

DEATH OVERSEAS

Importation or Exportation of Human Remains

There are no federal restrictions on the importation of human remains, unless the cause of death was one of the following communicable diseases: cholera or suspected cholera, diphtheria, infectious tuberculosis, plague, suspected smallpox, yellow fever, or suspected viral hemorrhagic fevers (Lassa,

Marburg, Ebola, Congo-Crimean, or others not yet isolated or named). If the death was the result of one of these diseases, the remains must be cremated or properly embalmed; placed in a hermetically sealed casket; and be accompanied by a death certificate, translated into English, that states the cause of death. The local mortician handling the remains following their importation will be subject to the regulations of the state and local health authorities for interstate and intrastate shipment.

The United States has no requirements for the exportation of human remains; however, travelers should be advised that the requirements of the country of destination must be met. Travelers should also be advised that information regarding these requirements may be obtained from the appropriate embassy or local consulate general.

THE POST-TRAVEL PERIOD

Some diseases might not manifest themselves immediately. If travelers become ill after they return home, they should be advised to tell their physician where they have traveled.

Most travelers who acquire viral, bacterial, or parasitic infections abroad become ill within 6 weeks after returning from international travel. However, some diseases might not manifest themselves immediately; for example, malaria might not cause symptoms for as long as 6 months to a year after a traveler returns to the United States. The traveler should be advised to inform his or her physician of the countries visited within the 12 months preceding onset of illness. Knowledge of such travel and the possibility the traveler might be ill with a disease the physician rarely encounters will help the physician arrive at a correct diagnosis.

ANIMAL IMPORTATION AND REENTRY

Travelers should be advised that pets that are transported internationally should be free of communicable diseases that can be transmissible to humans. U.S. Public Health Service (PHS) regulations place the following restrictions on the importation of dogs, cats, nonhuman primates, and turtles.

Dogs

Dogs older than 3 months of age presented for importation from countries where rabies is known to occur (see Table 3-12) must be accompanied by a valid rabies vaccination certificate that includes the following information.

1. The breed, sex, age, color, markings, and other identifying information.

2. A vaccination date at least 30 pays prior to importation (see following).

3. The vaccination expiration date. If not shown, the date of vaccination must be within 12 months prior to importation.

4. The signature of a licensed veterinarian.

A dog not accompanied by the previously described certificate may be admitted, providing the importer completes a confinement agreement. Such a dog must be kept in confinement during transit to, and be vaccinated within 4 days of arrival at, the U.S. destination. Such a dog must remain in confinement for at least 30 days after the date of vaccination.

A dog younger than 3 months of age may be admitted, provided the importer completes a confinement agreement. Such a dog must be kept in confinement during transit and at the U.S. destination until it is vaccinated at 3 months of age and for at least 30 days after vaccination. Routine rabies vaccination of dogs is recommended in the United States and required by most state and local health authorities.

Cats

Although proof of rabies vaccination is not required for cats, routine rabies vaccination of cats is recommended in the United States and required by most state and local health authorities.

Monkeys and Other Nonhuman Primates

Nonhuman primates can transmit a variety of serious diseases to humans. Live monkeys and other nonhuman primates may be imported into the United States only by importers registered with the Centers for Disease Control and Prevention (CDC) and only for scientific, educational, or exhibition purposes. Monkeys and other nonhuman primates may not be imported for use as pets.

Turtles

Turtles can transmit salmonellosis to humans, and because small turtles are often kept as pets, restrictions apply to their importation. Live turtles with a carapace (shell) length of less than 4 inches and viable turtle eggs may be imported into the United States if the importation is not for commercial purposes. The PHS has no restrictions on the importation of live turtles with a carapace length of more than 4 inches.

Measures at Ports of Entry

PHS regulations provide for the examination of admissible dogs, cats, nonhuman primates, and turtles presented for importation into the United States. Animals with evidence of disease that might be transmissible to humans may be subject to additional disease control measures.

General

For additional information regarding importation of these animals, travelers should be advised to contact the Centers for Disease Control and Prevention, Attention: National Center for Infectious Diseases, Division of Quarantine, Mailstop E03, Atlanta, Georgia 30333 (1-404-639-8107).

Travelers planning to import horses, ruminants, swine, poultry, birds, and dogs used handling livestock should be advised to contact the U.S. Department of Agriculture (1-301-734-8364) regarding additional requirements.

Travelers planning to import fish, reptiles, spiders, wild birds, rabbits, bears, wild members of the cat family, or other wild or endangered animals should be advised to contact the U.S. Department of the Interior, Fish and Wildlife Service (1-703-358-1949).

Travelers planning to take a pet to a foreign country should be advised to meet the entry requirements of the country of destination. To obtain this information, travelers should write or call the country's embassy in Washington, D.C., or the nearest consulate.

Chapter 5

Geographic Distribution of Potential health hazards to Travelers

GEOGRAPHIC DISTRIBUTION OF POTENTIAL HEALTH HAZARDS TO TRAVELERS

This section[1] is intended to give a *broad* indication of the health risks to which travelers might be exposed in various areas of the world and which they might not encounter in their usual place of residence.

In practice, to identify areas accurately and define the degree of risk likely in each of them is extremely difficult, if not impossible. For example, viral hepatitis A is ubiquitous, but the risk of infection varies not only according to area but also according to eating habits; hence, there might be more risk from communal eating in an area of low incidence than from eating in a private home in an area of high incidence. Generalizations might, therefore, be misleading.

Another factor is that tourism is an important source of income for many countries and to label specific areas as being of high risk for a disease might be misinterpreted. However, this does not absolve national health administrations from their responsibility to provide an accurate picture of the risks from communicable diseases that might be encountered in various parts of their countries.

AFRICA

North Africa (Algeria, Egypt, Libya, Morocco, and Tunisia) is characterized by a generally fertile coastal area and a desert hinterland with oases that are often foci of infections.

Arthropod-borne diseases are unlikely to be a major problem to the traveler, although dengue fever, filariasis (focally in the Nile Delta), leishmaniasis, malaria, relapsing fever, Rift Valley fever, sand fly fever, typhus, and West Nile fever do occur in some areas.

Foodborne and waterborne diseases are endemic; the dysenteries and other diarrheal diseases are particularly common. Hepatitis A occurs throughout the area, and hepatitis E is endemic in some regions. Typhoid fever is common in some areas. Schistosomiasis is prevalent both in the Nile Delta area in Egypt and in the Nile valley; it occurs focally elsewhere in the area. Alimentary helminthic infections, brucellosis, and giardiasis are common. Echinococcosis (hydatid disease) can occur. Sporadic cases of cholera occur.

Other diseases. Poliomyelitis eradication efforts in northern Africa have been very successful and wild virus transmission in most of the area might have been interrupted. Egypt is the only country where confirmed cases of poliomyelitis were still reported in 1997. Trachoma and rabies are hazards in certain areas.

Other hazards: Snakes and scorpions are a hazard in certain areas.

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[1]This section has been adapted from International Travel and Health: Vaccination Requirements and Health Advice—Situation as on 1 January 2001, published by the World Health Organization. Therefore, some information in this chapter might not parallel precisely information in other chapters of this book or CDC recommendations.

Central, East, and West Africa (Angola, Benin, Burkina Faso, Burundi, Cameroon, Cape Verde Islands, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Djibouti, Equatorial Guinea, Eritrea, Ethiopia, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Niger, Nigeria, Réunion, Rwanda, São Tomé and Principe, Senegal, Seychelles, Sierra Leone, Somalia, Sudan, Togo, Uganda, Tanzania, Zambia, and Zimbabwe). In this area, entirely within the tropics, the vegetation varies from the tropical rain forests of the west and center to the wooded steppes of the east, and from the desert of the north through the Sahel and Sudan savannahs to the moist orchard savannah and woodlands north and south of the equator.

Many of the diseases listed in the following section occur in localized foci and are confined to rural areas. They are mentioned so that the international traveler and the medical practitioner concerned can be aware of the diseases that can occur.

Arthropod-borne diseases are a major cause of morbidity. Malaria in the severe *Plasmodium falciparum* form occurs throughout the area, except at over 2,600 meters (8,530 feet) altitude and in the islands of Réunion and the Seychelles. Various forms of filariasis are widespread; endemic foci of onchocerciasis (river blindness) exist in all the countries listed except in the greater part of Kenya and in Djibouti, The Gambia, Mauritania, Mozambique, Somalia, Zambia, Zimbabwe, and the island countries of the Atlantic and Indian Oceans. However, onchocerciasis exists on the island of Bioko, Equatorial Guinea. Both cutaneous and visceral leishmaniasis can be found, particularly in the drier areas. Visceral leishmaniasis is epidemic in eastern and southern Sudan. African sleeping sickness (African trypanosomiasis), in discrete foci, is reported in all countries except Djibouti, Eritrea, The Gambia, Mauritania, Niger, Somalia, and the island countries of the Atlantic and Indian Oceans. The transmission rate of trypanosomiasis is high in northwestern Uganda and very high in northern Angola, Democratic Republic of the Congo (mostly Equateur and Bandundu), and southern Sudan, and there is significant risk of infection for travelers visiting or working in rural areas. Relapsing fever and louse-, flea-, and tickborne typhus occur. Natural foci of plague[2] have been reported in Angola, Democratic Republic of the Congo, Kenya, Madagascar, Malawi, Mozambique, Uganda, Tanzania, Zambia, and Zimbabwe. Tungiasis (skin penetration by larva of the female sand flea) is widespread. Many viral diseases, some presenting as severe hemorrhagic fevers, are transmitted by mosquitos, ticks, sand flies, and the like (which are found throughout this region). Large outbreaks of yellow fever occur periodically in the unvaccinated population.

Foodborne and waterborne diseases are highly endemic. Alimentary helminthic infections; the dysenteries; typhoid fever; hepatitis A and E; and diarrheal diseases, including giardiasis, are widespread. Cholera is actively transmitted in many countries in this area. Dracunculiasis (Guinea worm) infection occurs in isolated foci. Paragonimiasis (oriental lung fluke) has been reported from Cameroon; Gabon; Liberia; and, most recently, from Equatorial Guinea. Echinococcosis (hydatid disease) is widespread in animal-breeding areas. Poliomyelitis is probably endemic in most countries

[2]A natural focus of plague is a strictly delimited area where ecological conditions ensure the persistence of plague in wild rodents (and occasionally other animals) for long periods of time, and where epizootics and periods of quiescence may alternate.

except in Cape Verde, Comoros, Mauritius, Réunion, and the Seychelles. Schistosomiasis is present throughout the area except in Cape Verde, Comoros, Djibouti, Réunion, and the Seychelles.

Other diseases. Hepatitis B is hyperendemic. Trachoma is widespread. Among other diseases, certain, frequently fatal, Arenavirus hemorrhagic fevers have attained notoriety. Lassa fever has a virus reservoir in a commonly found multimammate rat. Studies have shown that an appreciable reservoir exists in some rural areas of West Africa; travelers visiting these areas should be advised to take particular care to avoid rat-contaminated food or food containers, but the extent of the disease should not be exaggerated. The Ebola and Marburg hemorrhagic fevers are present, but reported only infrequently.

Epidemics of meningococcal disease can occur throughout tropical Africa, particularly in the savannah areas during the dry season. For example, in recent years, epidemic outbreaks of meningitis from *Neisseria meningititis* type A have occurred in Rwanda. Rabies is also a hazard in some areas.

Other hazards include snake bites.

Southern Africa (Botswana, Lesotho, Namibia, Saint Helena, South Africa, and Swaziland) varies physically from the Namib and Kalahari deserts to fertile plateaus and plains to the more temperate climate of the southern coast.

Arthropod-borne diseases such as Crimean-Congo hemorrhagic fever, malaria, plague, relapsing fever, Rift Valley fever, tick-bite fever, and typhus (mainly tickborne) have been reported from most of this area, except Saint Helena. However, except for malaria in certain areas, they are not likely to be major health problems for the traveler. Natural foci of plague have been reported in Botswana, Namibia, and South Africa. African sleeping sickness (African trypanosomiasis) can occur in Botswana and Namibia.

Foodborne and waterborne diseases are common in some areas, particularly amebiasis and typhoid fever. Hepatitis A occurs in this area. Schistosomiasis is endemic in Botswana, Namibia, South Africa, and Swaziland.

Other diseases: The southern African countries are on the verge of becoming poliomyelitis-free, and risk of contacting poliovirus is now low. Hepatitis B is hyperendemic. Rabies can be a hazard in some areas.

Other hazards include snake bites.

THE AMERICAS

North America (Canada, Greenland, Saint Pierre and Miquelon, and the United States [with Hawaii]) extends from the Arctic to the subtropical cays of the southern United States.

In 1994, an international commission certified the eradication of endemic wild poliovirus from the Americas. While ongoing surveillance in formerly endemic Central and South American countries confirms that wild poliovirus transmission remains interrupted, an outbreak of vaccine-derived type 1 poliovirus occurred in the Dominican Republic and Haiti in 2000.

The incidence of communicable diseases is such that they are unlikely to prove a hazard for international travelers greater than that found in their own country. There are, of course, health risks, but, in general, the precautions are minimal. Certain diseases occasionally occur, such as plague, rabies in wildlife (including bats), Rocky Mountain spotted fever, tularemia, arthropod-borne encephalitis, and seasonal outbreaks of influenza. Rodent-borne hantavirus has been identified, predominantly in the western states of the United States and in the southwestern provinces of Canada. Recently, cases of West Nile fever have occurred in the United States with the focus around the New York City area. Lyme disease is endemic in the northeastern, mid-Atlantic, and midwestern United States. Occasional cases have been reported from the Pacific Northwest. During recent years, the incidence of certain food-borne diseases (for example, salmonellosis) has increased in some regions. Other hazards include poisonous snakes, poison ivy, and poison oak. In the north, a serious hazard is the very low temperature in the winter.

In the United States, proof of immunization against diphtheria, measles, poliomyelitis, and rubella is now universally required for entry into school. In addition, the school entry requirements of most states include immunization against tetanus (49 states), pertussis (44 states), mumps (46 states), and hepatitis B (29 states).

Mexico and Central America (Belize, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, and Panama) ranges from the deserts of the north to the tropical rain forests of the southeast.

Of the *arthropod-borne diseases*, malaria and cutaneous and mucocutaneous leishmaniasis occur in all eight countries. Visceral leishmaniasis occurs in El Salvador, Guatemala, Honduras, Mexico, and Nicaragua. Onchocerciasis (river blindness) is found in two small foci in the south of Mexico and four dispersed foci in Guatemala. Chagas' disease (American trypanosomiasis) has been reported to occur in localized foci in rural areas in all eight countries. Bancroftian filariasis is present in Costa Rica. Dengue fever and Venezuelan equine encephalitis can occur in all countries.

Foodborne and waterborne diseases, including amebic and bacillary dysenteries and other diarrheal diseases, and typhoid fever are very common throughout the area. All countries except Panama reported cases of cholera in 1996. Hepatitis A occurs throughout the area, and hepatitis E has been reported in Costa Rica, Honduras, and Panama. Brucellosis occurs in the northern part of the area. Many *Salmonella typhi* infections from Mexico and *Shigella dysenteriae* type 1 infections from mainland Middle America as a whole have been caused by drug-resistant enterobacteria.

Other diseases. Rabies in animals (usually dogs and bats) is widespread throughout the area.

Other hazards: Snakes can be a hazard in some areas.

The Caribbean (Anguilla, Antigua and Barbuda, Aruba, Bahamas, Barbados, Bermuda, Cayman Islands, Cuba, Dominica, Dominican Republic, Grenada, Guadeloupe, Haiti, Jamaica, Martinique, Montserrat, Netherlands Antilles, Puerto Rico, Saint Kitts (Saint Christopher) and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Trinidad and Tobago, Turks and Caicos Islands, Virgin Islands [U.K], and Virgin Islands [U.S.]). The islands, a number of them mountainous with peaks 1,000 to 2,500 meters (3,281 to 8,202 feet) high, have an equable tropical climate with heavy rainstorms and high winds at certain times of the year.

Of the *arthropod-borne diseases*, malaria occurs in endemic form only in Haiti and in parts of the Dominican Republic. Diffuse cutaneous leishmaniasis was recently discovered in the Dominican Republic. Bancroftian filariasis occurs in Haiti, the Dominican Republic, and some other islands, and other filariases can occasionally be found. Human fascioliasis due to *Fasciola hepatica* is endemic in Cuba. Outbreaks of dengue fever occur in the area, and dengue hemorrhagic fever has also occurred. Tularemia has been reported from Haiti.

Of the *foodborne and waterborne diseases*, bacillary and amebic dysenteries are common, and hepatitis A is reported, particularly in the northern islands. No cases of cholera have been reported in the Caribbean. Schistosomiasis is endemic in the Dominican Republic, Guadeloupe, Martinique, Puerto Rico, and Saint Lucia, in each of which control operations are in progress. It can also occur sporadically in other islands. Animal rabies, particularly in the mongoose, is reported from several islands.

Other hazards: Spiny sea urchins and coelenterates (coral and jellyfish) and snake bites can be hazards in some areas.

Tropical South America (Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Paraguay, Peru, Suriname, and Venezuela) covers the narrow coastal strip on the Pacific Ocean; the high Andean range with numerous peaks 5,000 to 7,000 meters (16,604 to 22,966 feet) high; and the tropical rain forests of the Amazon basin, bordered to the north and south by savannah zones and dry tropical forest or scrub.

Arthropod-borne diseases are an important cause of ill health in rural areas. Malaria occurs in all 10 countries or areas, as do Chagas' disease (American trypanosomiasis), and cutaneous and mucocutaneous leishmaniasis. There has been an increase of the latter in Brazil and Paraguay. Visceral leishmaniasis is endemic in northeast Brazil, with foci in other parts of Brazil; less frequent in Colombia and Venezuela; rare in Bolivia and Paraguay; and unknown in Peru. Endemic onchocerciasis occurs in isolated foci in rural areas in Ecuador, Venezuela, and northern Brazil. Bancroftian filariasis is endemic in parts of Brazil, Guyana, and Suriname. Plague has been reported in natural foci in Bolivia, Brazil, Ecuador, and Peru. Among the arthropod-borne viral diseases, jungle yellow fever can be found in forest areas in all countries except Paraguay and areas east of the Andes; in Brazil it is confined to the northern and western states. Epidemics of viral encephalitis and dengue fever occur in some countries in this area. Bartonellosis, or Oroya fever (a sand fly-borne disease), occurs in arid river valleys on the western slopes of the Andes up to 3,000 meters (9,842 feet). Louse-borne typhus is often found in mountain areas of Colombia and Peru.

Foodborne and waterborne diseases are common and include amebiasis, diarrheal diseases, helminthic infections, and hepatitis A. Schistosomiasis is found in Brazil, Suriname, and north-central Venezuela. Paragonimiasis (oriental lung fluke) has been reported from Ecuador, Peru, and Venezuela. Brucellosis is common and echinococcosis (hydatid disease) occurs, particularly in Peru. Bolivia, Brazil, Colombia, Ecuador, Peru, and Venezuela all reported autochthonous cases of cholera in 1996.

Other diseases include rodent-borne Arenavirus hemorrhagic fever in Bolivia and Venezuela, and hepatitis B and D (delta hepatitis), which are highly endemic in the Amazon Basin. Rabies has been reported from many of the countries in this area. Outbreaks of meningococcal disease have been reported.

Other hazards: Snakes and leeches can be a hazard in some areas.

Temperate South America (Argentina, Chile, Falkland Islands [Malvinas], and Uruguay). The mainland ranges from the Mediterranean climatic area of the western coastal strip over the Andes divide on to the steppes and desert of Patagonia in the south and to the prairies of the northeast.

Arthropod-borne diseases are relatively unimportant except for the occurrence of Chagas' disease (American trypanosomiasis). Outbreaks of malaria occur in northwestern Argentina, and cutaneous leishmaniasis is reported from the northeastern part of the country.

Of the *foodborne and waterborne diseases*, gastroenteritis (mainly salmonellosis) is relatively common in Argentina, especially in suburban areas and among children younger than 5 years of age. Some cases of cholera were reported in Argentina in 1996. Typhoid fever is not very common in Argentina, but hepatitis A and intestinal parasitosis are widespread (the latter especially in the coastal region). Taeniasis (tapeworm), typhoid fever, viral hepatitis, and echinococcosis (hydatid disease) are reported from other countries.

Other diseases. Anthrax is an occupational hazard in the three mainland countries. Animal rabies is endemic in Argentina and Chile. Epidemic meningococcal disease has been reported in Chile. Rodent-borne hantavirus pulmonary syndrome has been identified in the north-central and southwestern regions of Argentina and in Chile.

ASIA

East Asia (China [including Hong Kong and Macao Special Administration Region], North Korea, Japan, Mongolia, South Korea, and Taiwan). The area includes the high mountain complexes, the desert and the steppes of the west, the various forest zones of the east, down to the subtropical forests of the southeast.

Among the *arthropod-borne diseases*, malaria occurs in China and the Korean peninsula. Although reduced in distribution and prevalence, bancroftian and brugian filariasis are still reported in southern China. A resurgence of visceral leishmaniasis is occurring in China. Cutaneous leishmaniasis has been

recently reported from Xinjiang, Uygur Autonomous Region. Plague can be found in China and Mongolia. Hemorrhagic fever with renal syndrome (rodent-borne Korean hemorrhagic fever) is endemic except in Mongolia, and epidemics of dengue fever and Japanese encephalitis can occur in some countries. Mite-borne or scrub typhus can be found in scrub areas in southern China, certain river valleys in Japan, and in South Korea.

Foodborne and waterborne diseases such as diarrheal diseases and hepatitis A are common in most countries. Hepatitis E is prevalent in western China. The present endemic area of schistosomiasis is in the central Chang Jiang (Yangtze) River basin in China; active foci no longer occur in Japan. Clonorchiasis (oriental liver fluke) and paragonimiasis (oriental lung fluke) are reported in China, including the Macao Special Administrative Region, and South Korea. Fasciolopsiasis (giant intestinal fluke) occurs in China, as does brucellosis. Cholera can occur in some countries in this area. Poliomyelitis eradication activities have rapidly reduced poliovirus transmission in East Asia. Reliable surveillance data indicate that poliovirus transmission has been interrupted in China since 1994.

Other diseases. Hepatitis B is highly endemic. Trachoma and leptospirosis occur in China. Outbreaks of meningococcal disease occur regularly in Mongolia. Rabies is endemic in China and Korea.

Southeast Asia (Brunei, Cambodia, Indonesia, Laos, Malaysia, Burma [Myanmar], the Philippines, Singapore, Thailand, and Vietnam). From the tropical rain and monsoon forests of the northwest, the area extends through the savannah and the dry tropical forests of the Indochina peninsula, returning to the tropical rain and monsoon forests of the islands bordering the South China Sea.

Arthropod-borne diseases are an important cause of morbidity throughout the area. Malaria and filariasis are endemic in many parts of the rural areas of all the countries or areas—except for malaria in Brunei and Singapore, where normally only imported cases occur. In Brunei, the common arthropod-borne diseases such as filariasis, dengue, hemorrhagic fever, and Japanese encephalitis are nonendemic. Natural foci of plague have been reported in Indonesia, Burma (Myanmar), and Vietnam. Japanese encephalitis, dengue, and dengue hemorrhagic fever can occur in epidemics in both urban and rural areas. Mite-borne typhus has been reported in deforested areas in most countries.

Foodborne and waterborne diseases are common. Cholera and other watery diarrheas, amebic and bacillary dysentery, typhoid fever, and hepatitis A and E can occur in all countries in the area. Schistosomiasis is endemic in the southern Philippines and in central Sulawesi (Indonesia) and occurs in small foci in southern Laos and Cambodia. Among helminthic infections, fasciolopsiasis (giant intestinal fluke) can be acquired in most countries in the areas; clonorchiasis (oriental liver fluke) in the Indochina peninsula; opisthorchiasis (cat liver fluke) in the Indochina peninsula, the Philippines, and Thailand; and paragonimiasis in most countries. Melioidosis can occur sporadically throughout the area. The only remaining focus of poliovirus transmission is in the Mekong Delta

area of Cambodia and southern Vietnam. Poliovirus transmission has probably been interrupted in Indonesia, Laos, Malaysia, Burma (Myanmar), the Philippines, and Thailand.

Other diseases. Hepatitis B is highly endemic. Trachoma exists in Indonesia, Burma (Myanmar), Thailand, and Vietnam. Rabies has been reported.

Other hazards include snake bites and leeches.

Indian Subcontinent, West Central Asia, Some Middle East, and Eastern Europe (Afghanistan, Armenia, Azerbaijan, Bangladesh, Bhutan, Georgia, India, Iran, Kazakhstan, Kyrgyzstan, Maldives, Nepal, Pakistan, Sri Lanka, Tajikistan, Turkmenistan, and Uzbekistan). Bordered for the most part by high mountain ranges in the north, the area extends from steppes and desert in the west to monsoon and tropical rain forests in the east and south.

Arthropod-borne diseases are endemic in all these countries except for malaria in Kazakhstan, Krygyzstan, Maldives, and Uzbekistan. There are small foci of malaria in Armenia, Azerbaijan, Georgia, Tajikistan, and Turkmenistan. In some other countries, malaria occurs in urban as well as rural areas. Filariasis is common in Bangladesh, India, and the southwestern coastal belt of Sri Lanka. Sand fly fever is on the increase. A sharp rise in the incidence of visceral leishmaniasis has been observed in Bangladesh, India, and Nepal. In Pakistan, it is mainly reported from the north (Baltisan). Cutaneous leishmaniasis occurs in Afghanistan, India (Rajasthan), Iran, and Pakistan. There are very small foci of cutaneous and visceral leishmaniasis in Azerbaijan and Tajikistan. There is evidence that natural foci of plague exist in India and Kazakhstan. Tickborne relapsing fever is reported from Afghanistan, India, and Iran, and typhus occurs in Afghanistan and India. Outbreaks of dengue fever can occur in Bangladesh, India, Pakistan, and Sri Lanka, and the hemorrhagic form has been reported from eastern India and Sri Lanka. Japanese encephalitis has been reported from the eastern part of the area and Crimean-Congo hemorrhagic fever from the western part. Another tickborne hemorrhagic fever has been reported in forest areas of Karnataka State in India and in a rural area of Rawalpindi District in Pakistan.

Foodborne and waterborne diseases are common throughout the area, in particular cholera and other watery diarrheas, the dysenteries, typhoid fever, hepatitis A and E, and helminthic infections. Large epidemics of hepatitis E can occur. Giardiasis is common in the area. A very limited focus of urinary schistosomiasis persists in southwest Iran. Brucellosis and echinococcosis (hydatid disease) are found in many countries in the area. Poliomyelitis eradication activities have begun in all countries in the area, rapidly reducing the risk of infection with wild poliovirus. However, surveillance data are incomplete and poliovirus transmission should still be assumed to be a risk to travelers in most countries, especially in the Indian subcontinent.

Other diseases. Hepatitis B is endemic. Outbreaks of meningococcal disease have been reported in Afghanistan, India, and Nepal. Trachoma is common in Afghanistan, in parts of India, Iran, Nepal, and Pakistan. Rabies is present in animals.

Other hazards. Snakes are hazards in most of the countries in the area.

Middle East (Bahrain, Cyprus, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Syria, Turkey, United Arab Emirates, and Yemen). The area ranges from the mountains and steppes of the northwest to the large deserts and dry tropical scrub of the south.

Arthropod-borne diseases, except for malaria in certain areas, are not a major hazard for the traveler. Malaria does not exist in Kuwait and no longer occurs in Bahrain, Cyprus, Israel, Jordan, Lebanon, or Qatar. Its incidence in Oman, Syria, and United Arab Emirates is low, but elsewhere it is endemic in certain rural areas. A rise in West Nile Fever has been seen recently in Israel. A meningococcal vaccination certificate is required from all visitors arriving for the purpose of Umra or Hajj for seasonal work. Cutaneous leishmaniasis is reported throughout the area; visceral leishmaniasis, although rare throughout most of the area, is common in central Iraq, in the southwest of Saudi Arabia, in the northwest of Syria, in Turkey (southeast Anatolia only), and in the west of Yemen. Murine and tickborne typhus can occur in certain countries. Tickborne relapsing fever can occur. Crimean-Congo hemorrhagic fever has been reported from Iraq. Limited foci of onchocerciasis area reported in Yemen.

Foodborne and waterborne diseases are, however, a major hazard in most countries in the area. The typhoid fevers and hepatitis A exist in all countries. Schistosomiasis occurs in Iraq, Saudi Arabia, Syria, and Yemen. Dracunculiasis (guinea worm) occurs in isolated foci in Yemen. Taeniasis (tapeworm) is reported from many of the countries. Brucellosis is reported from most countries, and there are foci of echinococcosis (hydatid disease). The risk of poliovirus infection is low in most countries of the area, with the exception of Yemen. Trachoma and animal rabies are found in many countries in the area.

Other diseases. Hepatitis B is endemic.

Other hazards. The greatest hazards to pilgrims to Mecca and Medina are heat and dehydration if the period of the Hajj coincides with the hot season.

EUROPE

Eastern and Western Europe (Belarus, Belgium, Czech Republic, Denmark [with the Faroe Islands], Estonia, Finland, Germany, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Moldova, Russia, Slovakia, Sweden, Ukraine, and the United Kingdom [with the Channel Islands and the Isle of Man].) The area encompassed by these countries extends from the broadleaf forests and the plains of the west to the boreal and mixed forest to be found as far east as the Pacific Ocean.

The incidence of communicable diseases in most countries is such that they are unlikely to prove a hazard to international travelers greater than that found in their own country. There are, of course, health risks, but in most areas very few precautions are required.

Of the *arthropod-borne diseases*, there are very small foci of tickborne typhus in east and central Siberia. Tickborne encephalitis, for which a vaccine exists, and Lyme disease can occur throughout

forested areas where the vector ticks are found infective (for example, in the Baltic states, neighboring forested areas of Russia, and some forested areas in central and eastern Europe). Rodent-borne hemorrhagic fever with renal syndrome is now recognized as occurring at low endemic levels in this area.

Foodborne and waterborne diseases reported, other than the ubiquitous diarrheal diseases, are taeniasis (tapeworm) and trichinellosis in parts of northern Europe, and diphyllobothriasis (fish tapeworm) from the freshwater fish around the Baltic Sea area. *Fasciola hepatica* infection can occur. Hepatitis A occurs in the eastern European countries. The incidence of certain foodborne diseases (for example, salmonellosis and campylobacteriosis) is increasing significantly in some of these countries. All endemic countries in the area are now making intense efforts to eradicate poliomyelitis.

Other diseases. Rabies is endemic in wild animals (particularly foxes) in rural areas of northern Europe. In recent years, Belarus, Russia, and Ukraine have experienced extensive epidemics of diphtheria. Diphtheria cases, mostly imported from these three countries, have also been reported from neighboring countries: Estonia, Finland, Latvia, Lithuania, Poland, and Moldova.

Other hazards. The extreme cold in winter is a climatic hazard in parts of northern Europe.

Eastern and Western Europe (Albania, Andorra, Austria, Bosnia and Herzegovina, Bulgaria, Croatia, France, Gibraltar, Greece, Hungary, Italy, Liechtenstein, Malta, Monaco, Portugal [with the Azores and Madeira], Romania, San Marino, Slovenia, Spain [with the Canary Islands], Switzerland, the Former Yugoslav Republic of Macedonia, and Yugoslavia). The area extends from the broadleaf forests in the northwest and the mountains of the Alps to the prairies and, in the south and southeast, the scrub vegetation of the Mediterranean.

Among the *arthropod-borne diseases*, sporadic cases of murine and tickborne typhus and mosquito-borne West Nile fever occur in some countries bordering the Mediterranean littoral. Both cutaneous and visceral leishmaniasis and sand fly fever are also reported from this area. *Leishmania* and human immunodeficiency virus (HIV) co-infections have been reported from France, Greece, Italy, Portugal, and Spain. Tickborne encephalitis, for which a vaccine exists; Lyme disease; and rodent-borne hemorrhagic fever with renal syndrome can occur in the eastern and southern parts of the area.

Foodborne and waterborne diseases, such as bacillary dysentery and other diarrheas, and typhoid fever, are more common in the summer and autumn months, with a high incidence in the southeastern and southwestern parts of the area. Brucellosis can occur in the extreme southwest and southeast and echinococcosis (hydatid disease) in the southeast. Fasciola hepatica infection has been reported from different countries in the area. Hepatitis A occurs in the eastern European countries. The incidence of certain foodborne diseases (for example, salmonellosis and campylobacteriosis) is increasing significantly in some of these countries. All countries in southern Europe where poliomyelitis was until recently endemic are conducting eradication activities, and the risk of infection in most countries is very low. However, a large poliomyelitis outbreak occurred in 1996 in Albania; also affecting Greece and Yugoslavia, it had been interrupted by the end of 1996.

Other diseases. Hepatitis B is endemic in the southern part of eastern Europe (Albania, Bulgaria, and Romania). Rabies in animals exists in most countries of southern Europe.

OCEANIA

Australia, New Zealand, and the Antarctic. In Australia, the mainland has tropical monsoon forests in the north and east; dry tropical forests, savannah, and deserts in the center; and Mediterranean scrub and subtropical forests in the south. New Zealand has a temperate climate with the North Island characterized by subtropical forests and the South Island by steppe vegetation and hardwood forests.

International travelers to Australia and New Zealand will, in general, not be subjected to the hazards of communicable diseases to an extent greater than that found in their own country.

Arthropod-borne diseases (mosquito-borne epidemic polyarthritis and viral encephalitis) can occur in some rural areas of Australia. Occasional outbreaks of dengue have occurred in northern Australia in recent years.

Other hazards. Coelenterates (corals and jellyfish) might prove a hazard to the sea-bather, and heat is a hazard in the northern and central parts of Australia. Insectivorous and fruit-eating bats in Australia have been found to harbor a virus related to rabies virus and, therefore, should be avoided. Snakes and poisonous spiders are a hazard in most parts of the country. Large crocodiles inhabit almost all rivers and estuaries in the tropical north of Australia. People should avoid walking or swimming in bodies of water in this area at all times.

Melanesia and Micronesia–Polynesia (American Samoa, Cook Islands, Easter Island, Federated States of Micronesia, Fiji, French Polynesia, Guam, Kiribati, Marshall Islands, Nauru, New Caledonia, Niue, Palau, Papua New Guinea, Pitcairn Islands, Samoa, Solomon Islands, Tokelau, Tonga, Trust Territory of the Pacific Islands, Tuvalu, Vanuatu, Wake Island [U.S.], and the Wallis and Futuna Islands). The area covers an enormous expanse of ocean with the larger, mountainous, tropical and monsoon rainforest-covered islands of the west giving way to the smaller, originally volcanic peaks and coral islands of the east.

Arthropod-borne diseases occur in the majority of the islands. Malaria is endemic in Papua New Guinea, Solomon Islands, and Vanuatu. Filariasis is widespread, but its prevalence varies. Mite-borne typhus has been reported from Papua New Guinea. Dengue fever, including it hemorrhagic form, can occur in epidemics in most islands.

Foodborne and waterborne diseases such as the diarrheal diseases, typhoid fever, and helminthic infections are commonly reported. Biointoxication can occur from raw or cooled fish and shellfish. Hepatitis A occurs in this area.

Other diseases. Hepatitis B is endemic. Poliomyelitis cases have not been reported from any of these areas for more than 5 years. Trachoma occurs in parts of Melanesia.

Other hazards: Coelenterates, poisonous fish, and sea snakes are a hazard to bathers.

CHAPTER 6

ADVISING THE TRAVELER WITH SPECIAL NEEDS

General Information Regarding Human Immunodeficiency Virus and Travel

Acquired immunodeficiency syndrome (AIDS), caused by the human immunodeficiency virus (HIV), has a very long and variable incubation period, generally lasting for many years. Some people infected with HIV have remained asymptomatic for more than a decade. Currently, there is no vaccine to protect against infection with HIV. Although there is no cure for AIDS, treatments and prophylaxis for many opportunistic diseases associated with AIDS are available.

International travelers should be advised that some countries serologically screen incoming travelers (primarily those with extended visits, such as for work or study) and deny entry to people with AIDS and those whose test results indicate infection with HIV. Moreover, travelers carrying antiretroviral medication might be denied entry to some countries. People who intend to visit a country for a substantial period or to work or study abroad should be informed of the policies and requirements of the particular country. This information is usually available from the consular officials of the individual nations. An unofficial list that has been compiled by the U.S. Department of State can be found at the following Internet address: http://www.travel.state.gov/HIVtestingreqs.html.

Specific Precautions for HIV-Infected Travelers

Health care providers should advise HIV-infected travelers of the following:

1. Travel, particularly to developing countries, can carry significant risks for exposure to opportunistic pathogens for HIV-infected travelers, especially those who are severely immunosuppressed. Consultation with a health care provider or with experts in travel medicine will help in planning itineraries.

2. During travel to developing countries, HIV-infected travelers are at even higher risk for food and waterborne diseases than they are in the United States. Food and beverages—in particular, raw fruits and vegetables, raw or undercooked seafood or meat, tap water, ice made with tap water, unpasteurized milk and dairy products, and food and beverages purchased from street vendors—might be contaminated. Food and beverages that are generally safe include steaming hot foods, fruits that are peeled by the traveler personally, bottled (carbonated) beverages, hot coffee or tea, beer, wine, or water brought to a rolling boil for one minute. When local sources of water must be used and boiling is not practical, certain portable water filtration units, when used in conjunction with chlorine or iodine, can increase the safety of water. Some units are available that offer the effects of iodine treatment with filtration in the same unit. For more information about how to select a proper water filter, travelers should be advised to write to the Center for Disease Control and Prevention's (CDC) National Prevention Information Network for CDC's pamphlet, "You can prevent cryptosporidiosis: a guide for people with HIV infection" at P.O. Box 6003, Rockville, Maryland 20849-6003, or call 1-800-458-5231 or TTY 1-800-243-7012. International callers must dial 1-301-562-1098.

3. Waterborne infections can also result from swallowing water during recreational water activities. To reduce the risk of cryptosporidiosis and giardiasis, travelers should be advised to avoid swallowing water during swimming and to avoid swimming in water that might be contaminated (for example, with sewage or animal waste).

4. Prophylactic antimicrobal agents against travelers' diarrhea are not recommended routinely for HIV-infected travelers to developing countries. These agents have adverse effects and can promote the emergence of drug-resistant organisms. However, several studies have shown that prophylactic antimicrobials can reduce the risk of diarrhea in travelers, though none has involved an HIV-infected population. In selected circumstances (for example, a brief period of travel to an area where the risk of infection is very high), after weighing the potential risks and benefits, the health care provider and traveler might decide that prophylactic antibiotics are warranted.

   For travelers to whom prophylaxis is offered, fluoroquinolones such as ciprofloxacin (500 milligrams [mg] taken once a day), can be considered. Trimethoprim-sulfamethoxazole (TMP-SMX) (one double-strength tablet daily) has also been shown to be effective as a prophylactic agent against travelers' diarrhea, but drug resistance is now common in tropical areas. Travelers already taking TMP-SMX for prophylaxis against *Pneumocystis carinii* pneumonia (PCP) might receive some protection against travelers' diarrhea. Health care providers of HIV-infected travelers who are not already taking TMP-SMX should carefully consider prescribing this agent solely for diarrhea prophylaxis because of high rates of adverse reactions and anticipated future need for the agent (for example, for PCP treatment and prophylaxis).

5. All HIV-infected travelers to developing countries should be advised to carry an antimicrobial agent (for example, ciprofloxacin, 500 mg twice a day for 3 to 7 days) with them to be taken as empirical therapy should diarrhea develop. Alternative antibiotics (for example, TMP-SMX) for empirical therapy for infants, children, adolescents, and pregnant women should be discussed. Travelers should be advised to consult a physician if the diarrhea is severe and does not respond to empirical therapy, if there is blood in the stool, if fever occurs with shaking chills, or if there is dehydration. Antiperistaltic agents (for example, diphenoxylate [Lomotil] and loperamide [Imodium]) are used to relieve the symptoms of diarrhea; however, they should not be used by travelers with high fever or with blood in the stool; these drugs should be discontinued if symptoms persist beyond 48 hours. These drugs are not recommended for HIV-positive infants, children, or adolescents.

6. Travelers should be advised about other preventive measures appropriate for anticipated exposures, such as malaria chemoprophylaxis, protection against arthropod vectors, immune globulin, and vaccination. Travelers should avoid direct skin contact with soil and sand (for example, by wearing shoes and protective clothing, and using towels on beaches) in areas where fecal contamination of soil is likely.

7. In general, live virus vaccines should be avoided. An exception is measles vaccine, which is recommended for nonimmune travelers. However, measles vaccine is not recommended for travelers who are severely immunocompromised; immune globulin should be considered for

measles-susceptible, severely immunosuppressed travelers who are anticipating travel to measles endemic countries. Travelers at risk for exposure to typhoid fever should be given the inactivated parenteral typhoid vaccine, instead of the live, attenuated oral typhoid vaccine. Yellow fever vaccine is a live virus vaccine with uncertain safety and efficacy in those who are HIV infected. Travelers with asymptomatic HIV infection who cannot avoid potential exposure to yellow fever should be offered the choice of vaccination. If travel to a yellow fever-infected zone is necessary and immunization is not performed, travelers should be advised of the risk, instructed in methods to avoid bites of vector mosquitoes, and provided a vaccination waiver letter.

8. In general, killed vaccines (for example, diphtheria-tetanus, hepatitis A, rabies, and Japanese encephalitis vaccines) should be used for HIV-infected travelers, just as they would be used for non-HIV-infected travelers. Preparation for travel should include a review and updating of routine vaccinations, including diphtheria-tetanus in adults and routine immunizations for infants, children, and adolescents.

9. Health care providers should identify other area-specific risks and instruct travelers in ways to reduce the risk of infection. Geographically focal infections that pose high risk to HIV-infected travelers include: visceral leishmaniasis and several fungal infections (for example, *Penicillium marneffei*, coccidioidomycosis, and histoplasmosis). Many tropical and developing areas of the world have high rates of tuberculosis. (See Chapter 3, "Specific Recommendations for Vaccinations and Disease Prevention," "Tuberculosis," pages 144 through 146.)

Vaccine Recommendations for Travelers With Altered Immunocompetence, Including HIV

Killed or inactivated vaccines do not represent a danger to immunocompromised travelers and generally should be administered as recommended for healthy travelers. However, the immune response to these vaccines might be suboptimal.

Virus replication after administration of live, attenuated virus vaccines can be enhanced and prolonged in travelers with immunodeficiency diseases and in those with a suppressed capacity for immune response, as occurs with HIV disease; leukemia; lymphoma; generalized malignancy; or therapy with corticosteroids, alkylating agents, antimetabolites, or radiation. Severe complications have been reported following vaccination with live, attenuated virus vaccines (for example, measles and polio) and with live bacterial vaccines (for example, Bacille Calmette-Guerin [BCG]) in patients with HIV disease, leukemia, and lymphoma or other people with suppressed capacity for immune response. In general, travelers with such conditions should not be given live organism vaccines.

Evidence based on case reports has linked measles vaccine virus infection to subsequent death in six severely immunosuppressed persons. For this reason, travelers who are severely immunosuppressed for any reason should not be given measles, mumps, and rubella (MMR) combined vaccine. Healthy, susceptible close contacts of severely immunosuppressed travelers may be vaccinated. MMR and other measles-containing vaccines are not recommended for HIV-infected travelers with evidence of severe immunosuppression (for example, travelers with a very low CD+4 T-lymphocyte count),

primarily because of the report of a case of measles pneumonitis in a measles vaccinee who had an advanced case of AIDS. Refer to the 1998 Advisory Committee on Immunization Practices (ACIP) statement on MMR for additional details on vaccination of travelers with symptomatic HIV infection.

Measles disease can be severe in people with HIV infection. MMR vaccine is recommended for all asymptomatic HIV-infected travelers and should be considered for symptomatic travelers who are not severely immunosuppressed. Asymptomatic infants, children, and adolescents do not need to be evaluated and tested for HIV infection before MMR or other measles-containing vaccines are administered. A theoretical risk of an increase (probably transient) in HIV viral load following MMR vaccination exists because such an effect has been observed with other vaccines. The clinical significance of such an increase is not known.

In general, travelers receiving large daily doses of corticosteroids (>2 milligrams per kilogram [mg/kg] per day or >20 mg per day of prednisone) for 14 days or more should not receive MMR vaccine because of concern about vaccine safety. MMR and its component vaccines should be avoided for at least one month after cessation of high-dose therapy. Travelers receiving low-dose or short-course (fewer than 14 days) therapy; alternate-day treatment; maintenance physiologic doses; or topical, aerosol, intra-articular, bursal, or tendon injections may be vaccinated. Although travelers receiving high doses of systemic corticosteroids daily or on alternate days during an interval of less than 14 days generally can receive MMR or its component vaccines immediately after cessation of treatment, some experts prefer waiting until 2 weeks after completion of therapy.

Travelers receiving cancer chemotherapy or radiation who have not received chemotherapy for at least 3 months may receive MMR or its component vaccines.

Travelers with leukemia in remission whose chemotherapy has been terminated for at least 3 months and transplant recipients who are beyond the period of immunosuppression may receive live virus vaccines. Most experts agree that steroid therapy usually does not contraindicate administration of live virus vaccine when it is short term; low to moderate dose (less than 2 weeks); long-term, alternate-day treatment with short-acting steroids; maintenance physiologic doses (replacement therapy); or administered topically (that is, to the skin or eyes) by aerosol or by intra-articular, bursal, or tendon injection.

Infants and children infected with HIV should receive, on schedule, all the routinely recommended inactivated vaccines (that is, acellular pertussis [DTaP], *Haemophilus influenzae* type B [Hib], and hepatitis B vaccines) whether or not they are symptomatic. Inactivated poliovirus vaccine (IPV) is the polio vaccine of choice for HIV-infected asymptomatic and symptomatic travelers and their household members and other close contacts. Pneumococcal vaccine is recommended for anyone 6 months of age or older with HIV infection. Because influenza can result in serious illness and complications, vaccination against influenza is a prudent precaution in HIV-infected travelers. Varicella vaccine may be considered for asymptomatic HIV-infected travelers with CD4+ percentages $25% (CDC Class 1; that is, no evidence of suppression).

Because oral poliovirus vaccine (OPV) is no longer available, IPV should be used to immunize HIV-infected travelers and their household contacts.

Safety of Vaccines for HIV-Infected People

Scientists have reviewed the safety and efficacy of vaccines (such as those for measles, yellow fever, influenza, or pneumococcal pneumonia) in people with HIV infection or AIDS. No increased incidence of adverse reactions to inactivated vaccines has been noted in these people. However, administration of live organism vaccines can carry increased risks of adverse reactions (see especially the sections on "Measles," pages 121 through 124, and "Yellow Fever," pages 154 through 160, in Chapter 3, "Specific Recommendations for Vaccinations and Disease Prevention"). In addition, the likelihood of successful immune response is reduced in some HIV-infected people (depending on the degree of immunodeficiency). On the other hand, because of their immuno-deficiency, many HIV-infected people are at increased risk for complications of vaccine-preventable diseases. Thus, the risk-benefit balance usually favors administration of vaccines to HIV-infected people, especially inactivated vaccines. Administration of vaccines should be backed up by behaviors to prevent infections (for example, avoiding mosquito bites in yellow fever areas and avoiding exposure to people with measles or chickenpox).

PREGNANCY, BREAST-FEEDING, AND TRAVEL

Factors Affecting the Decision To Travel

When deciding to travel, a pregnant woman should be advised to consider the potential problems associated with international travel, as well as the quality of medical care available at her destination and during transit. According to the American College of Obstetrics and Gynecology, the safest time for a pregnant woman to travel is during the second trimester (18 through 24 weeks) when she usually feels best and is in least danger of experiencing a spontaneous abortion or premature labor. A woman in the third trimester should be advised to stay within 300 miles of home because of concerns about access to medical care in case of problems such as hypertension, phlebitis, or false premature labor. Pregnant women should be advised to consult with their heath care providers before making any travel decisions. (See Table 6-1 for information on relative contraindications to international travel during pregnancy.)

General Recommendations for Travel

Once a pregnant woman has decided to travel, a number of issues need to be considered prior to her departure. For instance, a pregnant woman should be advised to travel with at least one companion; she should also be advised that, during her pregnancy, her level of comfort might be adversely affected by traveling. Following are some guidelines for the pregnant traveler with regard to medical considerations.

GUIDELINES FOR THE PREGNANT TRAVELER

The pregnant traveler should be advised to:

- **T** Make sure, before traveling, that her health insurance is valid while abroad and during pregnancy, and that the policy covers a newborn should delivery take place. Also, a supplemental travel insurance policy and a prepaid medical evacuation insurance policy should be obtained, though most might not cover pregnancy-related problems.

- **T** Check medical facilities at her destination. For a woman in the last trimester, medical facilities should be able to manage complications of pregnancy, toxemia, and cesarean sections.

- **T** Determine beforehand whether prenatal care will be required abroad and, if so, who will provide it. The pregnant traveler should also make sure prenatal visits requiring specific timing are not missed.

- **T** Determine, prior to traveling, whether blood is screened for human immunodeficiency virus (HIV) and hepatitis B at her destination. The pregnant traveler and her companion(s) also should be advised to know their blood types.

Motor vehicle accidents are a major cause of morbidity and mortality for pregnant women. When available, safety belts should be fastened at the pelvic area. Lap and shoulder restraints are best; in most accidents, the fetus recovers quickly from the safety belt pressure. However, even after seemingly blunt, mild trauma, a physician should be consulted.

Typical problems of pregnant travelers are the same as those experienced by pregnant nontravelers: fatigue, heartburn, indigestion, constipation, vaginal discharge, leg cramps, increased frequency of urination, and hemorrhoids. Signs and symptoms that indicate the need for immediate medical attention are bleeding, passing tissue or clots, abdominal pain or cramps, contractions, ruptured membranes, excessive leg swelling, headaches, or visual problems.

Hepatitis E (HEV), which is not vaccine preventable, can be especially problematic for pregnant women, for whom there is a case fatality rate of 17% to 33%. Therefore, pregnant women should be advised the best preventive measures are to avoid potentially contaminated water and food, as with other enteric infections.

Breast-Feeding and Travel

The decision to travel internationally while nursing produces its own challenges. However, breast-feeding has nutritional and anti-infective advantages that serve an infant well while traveling.

Table 6-1.—Relative Contraindications to International Travel During Pregnancy.

TRAVELERS WITH OBSTETRICAL RISK FACTORS	TRAVELERS WITH GENERAL MEDICAL RISK FACTORS	TRAVELERS CONTEMPLATING TRAVEL TO POTENTIALLY HAZARDOUS DESTINATIONS
History of miscarriage. Incompetent cervix. History of ectopic pregnancy (ectopic with present pregnancy should be ruled out prior to travel). History of premature labor or premature rupture of membranes. History of or existing placental abnormalities. Threatened abortion or vaginal bleeding during present pregnancy. Multiple gestation in present pregnancy. History of toxemia, hypertension, or diabetes with any pregnancy. Primigravida at 35 years of age or older or 15 years of age or younger.	Valvular heart disease. History of thromboembolic disease. Severe anemia. Chronic organ system dysfunction that requires frequent medical interventions.	High altitudes. Areas endemic for or with ongoing outbreaks of life-threatening food- or insect-borne infections. Areas where cholroquine-resistant *Plasmodium falciparum* is endemic. Areas where live virus vaccines are required and recommended.

Therefore, breast-feeding should be advised. Moreover, exclusive breast-feeding relieves concerns about sterilizing bottles and about availability of clean water. Supplements are usually not needed by breast-fed infants younger than 6 months of age, and breast-feeding should be maintained as long as possible. If supplementation is considered necessary, powdered formula that requires recon-stitution with boiled water should be carried. For short trips, it may be feasible to carry an adequate supply of pre-prepared canned formula.

Nursing women may be immunized for maximum protection, depending on the travel itinerary, but consideration needs to be given to the neonate who cannot be immunized at birth and who would not gain protection against many infections (for example, yellow fever, measles, and meningococcal meningitis) through breast-feeding.

Neither inactivated nor live virus vaccines affect the safety of breast-feeding for mothers or infants. Breast-feeding does not adversely affect immunization and is not a contraindication to the

administration of any vaccines, including live virus vaccines, for breast-feeding women. Although rubella vaccine virus may be transmitted in breast milk, the virus usually does not infect the infant and, if it does, the infection is well tolerated. Breast-fed infants should be vaccinated according to routine recommended schedules.

Nursing women should be advised that their eating and sleeping patterns, as well as stress, will inevitably affect their milk output. They need to increase their fluid intake; avoid excess alcohol and caffeine; and, as much as possible, avoid exposure to tobacco smoke.

Specific Recommendations for Pregnancy and Travel

Routine Immunizations

Because of the theoretical risks to the fetus from maternal vaccination, the risks and benefits of each immunization should be carefully reviewed. Ideally, all women who are pregnant should be up to date on their routine immunizations. In general, pregnant women should be advised to avoid live vaccines and to avoid becoming pregnant within 3 months of having received one; however, no harm to the fetus has been reported from the accidental administration of these vaccines during pregnancy (see Table 6-2).

Diphtheria-Tetanus

The combination diphtheria-tetanus immunization should be given if the pregnant traveler has not been immunized within 10 years, although preference would be for its administration during the second or third trimester.

Measles, Mumps, and Rubella

The measles vaccine, as well as the measles, mumps, and rubella (MMR) vaccines in combination, are live virus vaccines and are contraindicated in pregnancy. However, in cases in which the rubella vaccine was accidentally administered, no complications have been reported. Because of the increased incidence of measles in children in developing countries, and because of the disease's communicability and its potential for causing serious consequences in adults, it is advisable to recommend that nonimmune women delay traveling until after delivery, when immunization can be given safely. If a pregnant woman has a documented exposure to measles, immune globulin should be given within a 6-day period to prevent illness.

Poliomyelitis

It is important for the pregnant traveler to be protected against poliomyelitis. Paralytic disease can occur with greater frequency when infection develops during pregnancy. Anoxic fetal damage has also been reported, with up to 50% mortality in neonatal infection. If not previously immunized, a pregnant woman should be advised to have at least two doses of vaccine before travel (day 0 and at

Table 6-2.—Vaccination During Pregnancy.

VACCINE		USE
Hepatitis A	Inactivated virus	Data on safety in pregnancy are not available; the theoretical risk of vaccination should be weighed against the risk of disease.
Hepatitis B	Recombinant or plasma-derived	If indicated
Immune globulins, pooled or hyperimmune	Immune globulin or specific globulin preparations	If indicated
Influenza	Inactivated whole virus or subunit	If indicated
Japanese encephalitis	Inactivated virus	Data on safety in pregnancy are not available; the theoretical risk of vaccination should be weighed against the risk of disease.
Measles	Live attenuated virus	Contraindicated
Meningococcal meningitis	Polysaccharide	If indicated
Mumps	Live attenuated virus	Contraindicated
Pneumococcal	Polysaccharide	If indicated
Polio, inactivated	Inactivated virus	If indicated
Rabies	Inactivated virus	If indicated
Rubella	Live attenuated virus	Contraindicated
Tetanus-diphtheria	Toxoid	If indicated
Typhoid (ViCPS)	Polysaccharide	If indicated
Typhoid (Ty21a)	Live bacterial	Data on safety in pregnancy are not available.
Varicella	Live attenuated virus	If indicated
Yellow fever	Live attenuated virus	If indicated

1 month). Despite being a live virus vaccine, the oral poliovirus vaccine (OPV) was recommended in the past when immediate protection was needed. However, OPV is no longer available. There is no convincing evidence of adverse effects of inactivated poliovirus vaccine (IPV) in pregnant women or developing fetuses. However, it is prudent to avoid polio vaccination of pregnant women unless immediate protection is needed.

Breast-feeding does not interfere with successful immunization against polio.

Hepatitis B

The hepatitis B vaccine may be administered during pregnancy. Pregnant travelers should be advised to consult with their health care providers.

Influenza

The influenza and pneumococcal vaccines should be given to pregnant women with chronic diseases or pulmonary problems. In general, women with serious underlying illnesses should be advised not to travel to developing countries when pregnant.

Travel-Related Immunization During Pregnancy

Yellow Fever

The yellow fever vaccine should not be given to a pregnant woman unless travel to an endemic or epidemic area is unavoidable. In these instances, the vaccine can be administered. Although concerns exist, no congenital abnormalities have been reported after administration of this vaccine to pregnant women.

If traveling to or transiting regions within a country where the disease is not a current threat but where policy requires a yellow fever vaccination certificate, pregnant travelers should be advised to carry a physician's waiver, along with documentation (of the waiver) on the immunization record. In general, pregnant women should be advised to postpone until after delivery (when vaccine can be administered without concern of fetal toxicity) travel to areas where yellow fever is a risk. However, a nursing mother should also delay travel because the neonate cannot be immunized because of the risk of vaccine-associated encephalitis.

Hepatitis A

Pregnant women without immunity to hepatitis A virus (HAV) need protection before traveling to developing countries. HAV is usually no more severe during pregnancy than at other times and does not affect the outcome of pregnancy. There have been reports, however, of acute fulminant disease in pregnant women during the third trimester, when there is also an increased risk of premature labor and fetal death. These events have occurred in women from developing countries and might have

been related to underlying malnutrition. HAV is rarely transmitted to the fetus, but this can occur during viremia or from fecal contamination at delivery. Immune globulin is a safe and effective means of preventing HAV, but immunization with one of the HAV vaccines gives a more complete and prolonged protection. The effect of these inactivated virus vaccines on fetal development is unknown, but the production methods for the vaccines are similar to that for IPV, which is considered safe during pregnancy.

Typhoid

The safety of the oral Ty21a typhoid vaccine in pregnancy is not known. It is not absolutely contraindicated during pregnancy, according to the Advisory Committee on Immunization Practices (ACIP). Nonetheless, the Vi capsular polysaccharide vaccine (ViCPS) injectable preparation is the vaccine of choice during pregnancy because it is inactivated and requires only one injection. With either of these, the vaccine efficacy (about 70%) needs to be weighed against the risk of disease.

Meningococcal Meningitis

The polyvalent meningococcal meningitis vaccine can be administered during pregnancy if the woman is entering an area where the disease is epidemic. Studies of vaccination during pregnancy have not documented adverse effects among either pregnant women or neonates. Based on data from studies involving the use of meningococcal vaccines and other polysaccharide vaccines administered during pregnancy, altering meningococcal vaccination recommendations during pregnancy is unnecessary.

Rabies

The cell-culture rabies vaccines may be given during pregnancy for either pre- or postexposure prophylaxis.

Japanese Encephalitis

No information is available on the safety of Japanese encephalitis vaccine during pregnancy. It should not be routinely administered during pregnancy, except when a woman must stay in a high-risk area. If not mandatory, travel to such areas should be delayed.

Miscellaneous

Bacille Calmette-Guerin (BCG) vaccine for the prevention of tuberculosis can theoretically cause disseminated disease and, thus, affect the fetus. The vaccine is not recommended. Skin testing for tuberculosis exposure before and after travel is preferable when the risk is high.

Malaria During Pregnancy

Malaria in pregnancy carries significant morbidity and mortality for both the mother and the fetus. Pregnant women should be advised to avoid travel to malarious areas if possible. Because no antimalarial agent is 100% effective, if pregnant women do travel to malarious areas, they should be advised to use personal protection measures. Pregnant women should remain indoors between dusk and dawn; however, if they are outdoors at night, they should wear light-colored clothing, long sleeves, long pants, and shoes and socks. Pregnant women should sleep in air-conditioned quarters or use screens and permethrin-impregnated bed nets.

Pyrethrum-containing house sprays or coils may also be used indoors if insects are a problem. Insect repellents containing N,N-diethylmetatoluamide (DEET) (<35%) as recommended for adults should be used sparingly. Nursing mothers should advised to carefully to wash repellents off their hands and breast skin prior to handling infants.

For pregnant women who travel to areas without chloroquine-resistant *Plasmodium falciparum*, chloroquine has been used for malaria chemoprophylaxis for decades with no documented increase in birth defects. For pregnant women who travel to areas with chloroquine-resistant *P. falciparum*, mefloquine should be recommended for chemoprophylaxis during the second and third trimesters. For women in their first trimester, experience suggests that mefloquine causes no significant increase in spontaneous abortions or congenital malformations if taken during this period.

Because of evidence that chloroquine and mefloquine are not associated with congenital defects, the Centers for Disease Control and Prevention (CDC) do not recommend that women planning pregnancy need to wait a specific period of time after their use before becoming pregnant. However, if women or their health care providers wish to decrease the amount of antimalarial drug in the body before conception, Table 6-3 provides information on the half-lives of selected antimalarial drugs. After 2, 4, and 6 half-lives, approximately 25%, 6%, and 2% of the drug remains in the body.

Nursing mothers should be advised to take the usual adult dose of antimalarial appropriate for the country to be visited. The amount of medication in breast milk will not protect the infant from malaria. Therefore, the breast-feeding child needs his or her own prophylaxis.

Any pregnant traveler returning with malaria should be treated as a medical emergency. Women who have traveled to areas that have chloroquine-resistant strains of *P. falciparum* should be treated as if they have illness due to chloroquine-resistant organisms. Because of the serious nature of malaria, quinine or intravenous quinidine should be used and should be followed by Fansidar®, or even doxycycline, despite concerns regarding potential fetal problems. Frequent glucose levels and careful fluid monitoring often require intensive care supervision.

Travelers' Diarrhea During Pregnancy

Pregnant travelers should be advised to exercise dietary vigilance while traveling during pregnancy because dehydration from travelers' diarrhea (TD) can lead to inadequate placental blood flow. They

Table 6-3.—Half-Lives of Selected Antimalarial Drugs.

DRUG	HALF-LIFE
Chloroquine	Can extend from 6 to 60 days
Mefloquine	2 to 3 weeks
Doxycycline	12 to 24 hours
Atovaquone	2 to 3 days
Proguanil	14 to 21 hours
Primaquine	4 to 7 hours
Sulfadoxine	150 to 200 hours
Pyrimethamine	80 to 95 hours

should also boil potentially contaminated water and avoid long-term use of iodine-containing purification systems. Iodine tablets can probably be used for travel up to several weeks, but congenital goiters have been reported in association with administration of iodine-containing drugs during pregnancy. Pregnant travelers should eat only well-cooked meats and pasteurized dairy products, while avoiding pre-prepared salads; this will help to avoid diarrheal disease, as well as infections such as toxoplasmosis and listeria, which can have serious sequelae in pregnancy. Pregnant women should be advised not to use prophylactic antibiotics for the prevention of TD.

Oral rehydration is the mainstay of TD therapy. Bismuth subsalicylate compounds are contra-indicated because of the theoretical risks of fetal bleeding from salicylates and teratogenicity from the bismuth. The combination of kaolin and pectin may be used, but loperamide should be used only when necessary. The antibiotic treatment of TD during pregnancy can be complicated. An oral third-generation cephalosporin may be the best option for treatment if an antibiotic is needed.

Breast-feeding is desirable during travel and should be continued as long as possible because of its safety and the resulting lower incidence of infant diarrhea. A nursing mother with TD should not stop breast-feeding, but should increase her fluid intake.

Air Travel During Pregnancy

Commercial air travel poses no special risks to a healthy pregnant woman or her fetus. The lowered cabin pressures (kept at the equivalent of 1,524 to 2,438 meters [5,000 to 8,000 feet]) affect fetal oxygenation minimally because of the fetal hemoglobin dissociation curve. Severe anemia (hemoglobin, 0.5 grams per deciliter [g/dL]), sickle-cell disease or trait, a history of thrombo-phlebitis, or placental problems are relative contraindications to flying; however, supplemental oxygen can be ordered in advance. Each airline has policies regarding pregnancy and flying; it is always safest

to check with the airline when booking reservations because some will require medical forms to be completed. Domestic travel is usually permitted until the pregnant traveler is in her 36th week of gestation, and international travel may be permitted until the 32nd week. A pregnant woman should be advised always to carry documentation stating her expected date of delivery.

An aisle seat at the bulkhead will provide the most space and comfort, but a seat over the wing in the midplane region will give the smoothest ride. A pregnant woman should be advised to walk every half hour during a smooth flight and flex and extend her ankles frequently to prevent phlebitis. The safety belt should always be fastened at the pelvic level. Fluids should be taken liberally because of the dehydrating effect of the low humidity in aircraft cabins.

Women traveling with neonates or infants should be advised to check with their pediatricians regarding any medical contraindictions to flying. Infants are particularly susceptible to pain with eustachian tube collapse during pressure changes. Breast-feeding during ascent and descent relieves this discomfort.

The Travel Health Kit During Pregnancy

Additions and substitutions to the usual travel health kit need to be made during pregnancy and nursing. Talcum powder, a thermometer, oral rehydration salts (ORS) packets, multivitamins, an antifungal agent for vaginal yeast, acetaminophen, insect repellent containing a low percentage of DEET, and a sunscreen with a high SPF should be carried. Women in their third trimesters may be advised to carry a blood pressure cuff and urine dipsticks so they can check for proteinuria and glucosuria, both of which would require attention. Antimalarial and antidiarrheal self-treatment medications should be evaluated individually, depending on the traveler, her trimester, the itinerary, and her health history. Most medications should be avoided, if possible.

TRAVELERS WITH DISABILITIES

The U.S. Architectural and Transportation Barriers Compliance Board (Access Board) produces or distributes, or both, a variety of publications for travelers with disabilities, at no cost. This information may be obtained by writing to Access Board, Suite 1000, 1331 F Street, N.W., Washington, D.C. 20004-1111, or by telephoning 1-800-872-2253 (voice) or 1-800-993-2822 (TTY). Information is also available at their website (http://www.access-board.gov). U.S. air carriers must comply with the U.S. laws and regulations regarding access for travelers with disabilities. U.S. companies or entities conducting programs or tours on cruise ships also have obligations regarding access for travelers with disabilities, even if the ship itself is of foreign registry. Up-to-date information regarding access abroad is more difficult to obtain.

INTERNATIONAL ADOPTIONS

General Information About International Adoptions

Approximately 15,000 infants and children from abroad are adopted each year by citizens of the United States. Infants and children from Asian nations (for example, China, Korea, India, Vietnam, Cambodia, and the Philippines), Central and South American countries (for example, Guatemala and Colombia), and eastern Europe (for example, Russia, Romania, and Ukraine) account for more than 90% of international infants and children adopted by U.S. citizens. To complete an international adoption and bring an infant or a child to the United States, a prospective parent or parents must fulfill the requirements set by the U.S. Immigration and Naturalization Service (INS), the foreign country in which the infant or child resides, and sometimes the state of residence of the adoptive parent or parents. The U.S. Immigration and Nationality Act (INA) is the U.S. immigration law regarding the issuance of visas to nationals of other countries, including infants or children adopted abroad or coming to the United States for adoption. Detailed information about the procedures and requirements for international adoptions is available on the U.S. Department of State (DoS) website at http://www.travel.state.gov/int'ladoption.html. Additional information about international adoption is also available at the INS website at http://www.ins.usdoj.gov.html.

The prospective adoptive parent or parents must comply with U.S. immigration procedures, initiated through the INS in the United States, to bring an adoptive child to the United States. Simply locating an infant or a child in a foreign country and going to the applicable U.S. embassy to obtain a visa for the infant or child will not meet these requirements. An infant or child cannot be brought to the United States without a visa, issuance of which is based on an INS-approved petition (Orphan Petition: form I-600 or I-600A). For more specific information about INS requirements, prospective adoptive parents should be advised to see U.S. Department of Justice INS brochure M-249Y, "The Immigration of Adopted and Prospective Adoptive Children." The INS also has a toll-free information number (1-800-755-0777) from which applicants may request copies of the brochure and obtain the telephone numbers of local INS offices throughout the United States. The INS suggests that, early in the preadoption process, the prospective adoptive parent or parents contact the INS office having jurisdiction over his, her, or their place of residence in the United States for information.

When the Orphan Petition has been approved, the adoptive parent or parents can apply for an immigrant visa (IR-3 for an infant or a child adopted abroad and IR-4 for an infant or a child adopted in the United States) at the appropriate U.S. consular office abroad. In addition to the approved I-600 or I-600A petition from the INS, the consular officer also requires specific documentation to conduct a visa interview and issue a visa. One of these requirements is the medical examination of the infant or child by a designated physician.

Overseas Medical Examination for International Adoptions

All immigrants (including infants and children adopted overseas by U.S. citizens) and refugees coming to the United States must have a medical examination overseas as part of the immigrant visa requirements. The examination must be performed by a panel physician. A panel physician is a physician who has been approved by the U.S. embassy or consulate to perform medical examinations for immigrant visas overseas in that country.

The medical examination focuses primarily on detecting certain serious contagious diseases that might be the basis for visa ineligibility; prospective adoptive parents should be advised not to rely on this medical examination to detect all possible disabilities and illnesses. If an infant or a child is found to have any of the illnesses or disabilities that might be the basis for visa ineligibility, the infant or child may still be issued a visa after the illness has been treated and is no longer contagious, or after a waiver of the visa eligibility has been approved by the INS. If the panel physician or the consular official notes that the infant or child has a serious disease or disability, the prospective parent or parents will be notified and asked if he or she or they wish to proceed with the infant or child's immigration.

The existing medical examination procedure consists of a brief physical examination and medical history. A chest radiograph examination for tuberculosis and blood tests for syphilis and human immunodeficiency virus (HIV) is required for immigrants 15 years of age or older. Applicants younger than 15 years of age are tested only if there is reason to suspect any of these diseases.

In 1996, a new subsection was added to the INA requiring for the first time that any person seeking an immigrant visa for permanent residency show proof of having received the recommended vaccines (as established by the Advisory Committee on Immunization Practices [ACIP] of the Centers for Disease Control and Prevention) before immigration. While this new subsection now applies to all immigrant infants and children entering the United States, international adoptees younger than 11 years of age have been exempted temporarily from the overseas immunization requirements. Adoptive parents are required to sign a waiver indicating their intention to comply with the immunization requirements within 30 days after the infant or child's arrival in the United States.

Additional information about the medical examination and the vaccination exemption for international adoptees who are 10 years of age or younger is available on the DoS website at http://www.travel.state.gov/children's_issues.html#adoption.

Recommendations for Follow-Up Medical Examination After Arrival

The varied geographic origins of internationally adopted infants and children, their unknown backgrounds before adoption (including parental history and living circumstances), and the

inadequacy of health care in many developing countries make appropriate medical evaluation of international adoptees a complex and important task.

Usually, an internationally adopted infant or child should be examined within 2 weeks of his or her arrival in the United States. If the infant or child is suffering from an acute illness or has a chronic condition that needs immediate attention, he or she should be examined as soon as possible. Prospective parents might wish to meet with a physician before adoption to review medical records, if available, or to discuss common medical issues involving adopted infants and children. Parents who have not met with a physician before adopting should notify their chosen physician when the infant or child arrives so they can review basic medical issues.

All adopted infants and children should have a complete physical examination and medical history (for many internationally adopted infants and children, previous medical records and histories might be limited or unavailable), and should have age-appropriate screening tests, including evaluation for possible anemia, vision and hearing impairments, and assessment of growth and development. International adoptees frequently have additional medical needs. In studies of internationally adopted infants and children, infectious diseases are among the most common medical diagnoses and have been found in as many as 60% of infants and children, depending on their country of origin. Because many of these infections can be asymptomatic, the diagnosis must be made by using screening tests in addition to medical histories and physical examinations. Some infectious diseases occur with sufficient frequency that all international adoptees should be examined for them; for other, less common infectious diseases, screening algorithms should be based on the prevalence of the specific diseases in the infant or child's country of origin or residence. Other important medical diagnoses include hearing loss and vision abnormalities, growth and developmental retardation, nutrition deficiencies, and congenital anomalies.

A good source of information and recommendations for the medical evaluation of adopted infants and children is the American Academy of Pediatrics (AAP), including the publication "2000 Red Book: Report of the Committee on Infectious Diseases, 25th edition," which has an excellent chapter on infectious disease screening recommendations for international adoptees ("The Medical Evaluation of Internationally Adopted Children for Infectious Diseases"). Another is the AAP policy statement, "Initial Medical Evaluation of an Adopted Child," published in "Pediatrics," Volume 88, Number 3, September 1991.

Internationally adopted infants and children frequently are not immunized or are underimmunized. These infants and children should receive necessary immunizations according to recommended schedules in the United States. Only written documentation should be accepted as evidence of prior immunization. In general, written records can be considered valid if the vaccines, dates of administration, number of doses, intervals between doses, and age of the patient at the time of immunization are comparable to the current U.S. schedule or World Health Organization recommendations. Although some vaccines with inadequate potency have been produced in other countries, most vaccines used worldwide are produced with adequate quality control standards and are reliable. However, immunization records for some internationally adopted infants and children, particularly those from orphanages, might not accurately reflect protection because of inaccurate or

unreliable records, lack of vaccine potency, poor nutritional status, or other problems. Existing data are inconclusive as to the existence and extent of the problem among infants and children with recorded doses of vaccines administered abroad, and additional studies using standardized methodologies are planned or in progress. The ACIP is also currently formulating a statement on general recommendations on vaccination for internationally adopted infants and children that will be considered for approval in February 2001. Health care providers may follow one of several approaches if there is a question as to whether vaccines were administered to an international adoptee or were immunogenic. Repeating the vaccinations is an acceptable option. Doing so is generally safe and avoids the need to obtain and interpret serological tests. If there is a desire to avoid unnecessary injections, judicious use of serological testing can be helpful to the health care provider in determining which immunizations might be needed.

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INDEX

INDEX

A

Acaricides, 106
Acellular pertussis vaccine
  Haemophilus influenza type b, 84
  recommended childhood immunization schedule, 15, 16, 20
Acquired Immunodeficiency Syndrome
  disease specific information, 57-9
  general information regarding HIV and travel, 201
  HIV-infected travelers, 201-5
  influenza vaccine, 99, 101
  MMR and other measles-containing vaccines, 124
  sexually transmitted diseases, 143
  vaccine safety for HIV-infected people, 211
  WHO blood transfusion guidelines for international travelers, 186-7
  yellow fever vaccine, 158
Acupuncture
  acquired immune deficiency syndrome, 58
  hepatitis B, 91
  hepatitis C, 96
Acute illness, vaccination during, 8
Adolescents
  diphtheria, tetanus, and pertussis, 72
  hepatitis A, 95
  hepatitis B vaccine, 93
  influenza, 98
  malaria, 112
  MMR vaccine and HIV, 123
  poliomyelitis, 131
  varicella, 150-2
Adoptions, international, 221-4
Advisory Committee on Immunization Practices (ACIP)
  diphtheria, tetanus, and pertussis, 71
  measles, 124
  rubella, 140
  U.S. Public Health Service recommendations, 17, 21
  varicella, 153
Aedes aegypti mosquitoes, 67
Afghanistan
  geographic distribution of potential health hazards, 200
  hepatitis E,
  malaria risk and prophylaxis, by country, 25
  poliomyelitis,
  yellow fever, by country, 25
Africa
  African sleeping sickness, 59-60
  cholera, 64
  dengue fever, 67
  filariasis, lymphatic, 82
  hepatitis B, 91
  hepatitis C, 96
  hepatitis E, 97
  Lassa fever, 102
  leishmaniasis, 103
  malaria, 107, 109, 117
  meningococcal disease, 125
  onchocerciasis (river blindness), 129
  plague, 130
  poliomyelitis, 132
  rabies, 134-5
  Rift Valley fever, 139
  schistosomiasis, 141-2
  typhoid fever, 147
  typhus fevers, 149-50
  yellow fever, 154-5, 159
African sleeping sickness, 59-60
AIDS, see Acquired Immunodeficiency Syndrome
Air pollution
  environmental effects, 177
  natural disasters and environmental hazards, 180
Albania
  encephalitis, tickborne, 81
  geographic distribution of potential health hazards, 202-3
  malaria risk and prophylaxis, by country, 25
  rabies, 135
  yellow fever, by country, 25
Algeria
  geographic distribution of potential health hazards, 193

malaria risk and prophylaxis, by country, 25
yellow fever, by country, 25
Alkylating drugs, 158
Alopecia, 95
Altitude illness, 178-9
Amantadine, 101
Amazon River basin
hepatitis B, 91, 93
malaria, 109, 117-8
Amebiasis, 60-1
American Academy of Pediatrics
diphtheria, tetanus, and pertussis, 71
Haemophilus influenzae type b, 85
varicella, 153
American trypanosomiasis, see Chagas' disease
Anaphylaxis
encephalitis, Japanese, 80
Haemophilus influenzae type b, 86
hepatitis A, 90
hepatitis B, 95
hypersensitivity to vaccine components, 9
influenza, 100
rabies, 135
Andorra
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 25
rabies, 135
yellow fever, by country, 25
Angola
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 25
plague, 130
poliomyelitis, 132
yellow fever, 25
Anguilla
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 25
yellow fever, by country, 25
Animal-associated hazards, 182-3
Animal importation or reentry
cats, 189
dogs, 189-90
general information, 189-90
monkeys and other nonhuman primates, 189
turtles, 189
Anopheles mosquitoes, 106, 109
Antarctica, 134
Antibody response, 7, 8, 12
Antigua
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 25
rabies, 135
yellow fever, by country, 25
Antimalarial drugs, see specific drug entry
Antimotility agents, 172
Antiviral drugs
influenza, 99, 101
Lassa fever, 102
Argentina
Chagas' disease, 63
geographic distribution of potential health hazards, 194
leishmaniasis, 103
malaria risk and prophylaxis, by country, 25
yellow fever, by country, 25
Armenia
geographic distribution of potential health hazards, 200
malaria risk and prophylaxis, by country, 26
rabies, 135
yellow fever, by country, 26
Aruba
geographic distribution of potential health hazards, 197
rabies, 135
Asia
cholera, 64
dengue, 67
dengue hemorrhagic fever, 67, 69
encephalitis, Japanese, 74-5
filariasis, lymphatic, 82
geographic distribution of potential health hazards, 198-200
hepatitis B, 91
hepatitis C, 96
hepatitis E, 97
leishmaniasis, 103
Lyme disease, 105-6
malaria, 107, 117-8

measles, 121
plague, 130
poliomyelitis, 132
rabies, 134-5
schistosomiasis, 141-2
typhoid fever, 147
typhus fevers, 149
yellow fever, 155
Atovaquone-proguanil, 115-7, 219
Australia
disinsection, 177
encephalitis, Japanese, 76
geographic distribution of potential health hazards, 203
hepatitis A, 88
hepatitis B, 93
hepatitis C, 96
hepatitis E, 97
human immunodeficiency virus, 58
leishmaniasis, 103
malaria risk and prophylaxis, by country, 26
rabies, 135
travelers' diarrhea, 168
typhus fevers, 149
yellow fever, by country, 26
Austria
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 26
yellow fever by country, 26
Azerbaijan
malaria risk and prophylaxis, by country, 26
yellow fever, by country, 26
Azores
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 26
yellow fever, by country, 26

B

Bacille Calmette-Guerin
measles vaccine, simultaneous administration, 159
yellow fever, simultaneous administration, 159
Bahamas
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 26
rabies, 135
yellow fever, by country, 26
Bahrain
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 26
rabies, 135
yellow fever, by country, 26
Bangladesh
encephalitis, Japanese, 76
geographic distribution of potential health hazards, 200
hepatitis E, 97
leishmaniasis, 103
malaria risk and prophylaxis, by country, 26
poliomyelitis, 132
yellow fever, by country, 26
Barbados
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 27
rabies, 137
yellow fever, by country, 27
Barbuda
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 25
rabies, 135
yellow fever, by country, 25
Bartonellosis, 197
Bed nets
encephalitis, Japanese, 80
leishmaniasis, 104
malaria, 109, 111
malaria during pregnancy, 218
protection against mosquitos and other arthropod vectors, 163-5
Belarus
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 27
yellow fever, by country, 27

Belgium
bovine spongiform encephalopathy, 61
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 27
yellow fever, by country, 27
Belize
geographic distribution of potential health hazards, 196
malaria risk and prophylaxis, by country, 27
yellow fever, by country, 27
Benin
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 27
yellow fever, by country, 27
Bermuda
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 27
rabies, 135
yellow fever, by country, 27
Bhutan
encephalitis, Japanese, 76
geographic distribution of potential health hazards, 200
malaria risk and prophylaxis, by country, 27
yellow fever, by country, 27
Bismuth subsalicylate, 171-2
Black flies, 129
Blood products
measles vaccine, 124
varicella vaccine, 153
Blood transfusion risks
Chagas' disease, 63
hepatitis B, 91
hepatitis C, 96
malaria, 106
World Health Organization guidelines, 186-7
Blue Sheet, 3, 21
Bolivia
geographic distribution of potential health hazards, 197-8
malaria risk and prophylaxis, by country, 28
plague, 130
rabies, 134
yellow fever, 154
yellow fever, by country, 28
Bosnia and Herzegovina
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 28
yellow fever, by country 28
Botswana
geographic distribution of potential health hazards, 195
plague, 130
malaria risk and prophylaxis, by country, 28
yellow fever, by country, 28
Bovine spongiform encephalopathy, 61-3
Brazil
geographic distribution of potential health hazards, 197-8
leishmaniasis, 103
malaria risk and prophylaxis, by country, 28
onchocerciasis, 129
plague, 130
rabies, 134
schistosomiasis, 141
yellow fever, 154
yellow fever, by country, 28
Breast-feeding
air travel, 220
influenza, 101
malaria, 116, 218
measles, 123
poliomyelitis, 133, 216
travel, 211-4
travelers' diarrhea, 219
typhoid vaccine, 18
varicella, 153
yellow fever vaccine, 216
British Virgin Islands
geographic distribution of potential health hazards, 197
rabies, 135
malaria risk and prophylaxis, by country, 51
yellow fever, by country 51
Brucellosis, 193, 196, 198-202
Brunei
encephalitis, Japanese, 76

geographic distribution of potential health hazards, 199
malaria risk and prophylaxis, by country, 29
rabies, 135
yellow fever, by country, 29
Bulgaria
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202-3
malaria risk and prophylaxis, by country, 29
yellow fever, by country, 29
Burkina Faso
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 29
yellow fever, by country, 29
Burundi
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 29
yellow fever, by country, 29

C

Cambodia
encephalitis, Japanese, 76
geographic distribution of potential health hazards, 199-200
malaria, 109, 112
malaria risk and prophylaxis, by country, 29
yellow fever, by country, 29
Cameroon
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 29
yellow fever, by country, 29
Campylobacter jejuni, 169
Canada
AIDS, 58
geographic distribution of potential health hazards, 195
malaria risk and prophylaxis, by country, 29
yellow fever, by country, 29
Canary Islands
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 29
yellow fever, by country, 29
Cape Verde
geographic distribution of potential health hazards, 194-5
malaria risk and prophylaxis, by country, 29
rabies, 135
yellow fever, by country, 29
Caribbean
disinsection of aircraft, 177
filariasis, lymphatic, 82
geographic distribution of potential health hazards, 197
hepatitis B, 91
malaria, 107
recreational water, 184
schistosomiasis, 142
travelers' diarrhea, 168, 170
Cayman Islands
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 30
rabies, 135
yellow fever, by country, 30
Central African Republic
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 30
yellow fever, by country, 30
Chad
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 30
yellow fever, by country, 30
Chagas' disease
disease-specific information, 63
geographic distribution of potential health hazards, 196-8
Chemoprophylaxis
filariasis, lymphatic, 82
influenza, 99
leptospirosis, 105

malaria, see Malaria
plague, 131
Chemotherapy
measles vaccine, 123, 210
varicella vaccine, 153
Chernobyl, 180-1
Chickenpox, see Varicella
Children
accelerated immunization schedule, 13
childhood immunization schedule, 14-5
immunization schedule for people older than 7 years of age, 19
initial vaccination age and minimum dose intervals, by vaccine, 20
malaria
drugs used in prophylaxis, 114-5
pediatric doses of Malarone™, 116
presumptive treatment, 118
Chile
geographic distribution of potential health hazards, 198
malaria risk and prophylaxis, by country, 30
yellow fever, by country, 30
China
encephalitis, Japanese, 74-5, 78
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 198-9
hepatitis B, 91
hepatitis E, 97
malaria risk and prophylaxis, by country, 30
plague, 130
poliomyelitis, 132
schistosomiasis, 141
typhus fevers, 149
yellow fever, by country, 30
Chloroquine
adverse reactions, 119
breast-feeding, 116
infants, children, and adolescents, 112-13
pregnancy, 113
prophylaxis, 109-11, 114-5
resistance, by country, 23-54
Cholera
death overseas, 187
disease-specific information, 64-5
emerging infectious diseases, 184
geographic distribution of potential health hazards, 193-4, 196-200
risks from food and drink, 165, 168
travelers' diarrhea, 170
vaccine, 64-5
Christmas Island
malaria risk and prophylaxis, by country, 30
yellow fever, by country, 30
Ciguatera fish poisoning, 168
Clonorchiasis, 199
Coccidioidomycosis, 209
Colombia
geographic distribution of potential health hazards, 197-8
malaria risk and prophylaxis, by country, 31
yellow fever, 154
yellow fever, by country, 31
Comoros
geographic distribution of potential health hazards, 194-5
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Congenital rubella syndrome, 140
Congo
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Cook Islands
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 31
rabies, 135
yellow fever, by country, 31
Corticosteroids, administration with
measles vaccine, 123
yellow fever, 158
Costa Rica
geographic distribution of potential health hazards, 196
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Côte d'Ivoire
geographic distribution of potential health hazards, 194

malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Cruetzfeldt-Jakob disease, see Bovine spongiform encephalitis
Crimean-Congo hemorrhagic fever, 195, 200-1
Croatia
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Cruise ship travel, 175-6
Cryptosporidiosis
disease-specific information, 65-6
food and drink, risks from, 165-7
HIV-infected travelers, specific precautions for, 207-8
travelers' diarrhea, 170, 184
Cuba
dengue hemorrhagic fever, 67
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Culex vishnui mosquitoes, 74
Cyclosporiasis, 66
Cyprus
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 31
rabies, 135
yellow fever, by country, 31
Czech Republic
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31

D

Death overseas, 187
DEET, see N,N-diethylmetatoluamide
Dehydration
travelers' diarrhea, 173-5, 218
HIV-infected travelers, 208
Dengue fever,
dengue hemorrhagic fever, 67-9, 197, 199
disease-specific information, 67-9
geographic distribution, 193, 196-7, 199, 200, 203
Denmark
bovine spongiform encephalopathy, 61
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Diamox, 179
Diphtheria
disease-specific information, 70-4
general recommendations on vaccination, 3, 6, 7, 12
geographic distribution of potential health hazards, 196, 202
HIV-infected travelers, 209
inadequately immunized infants and younger children, 12-3, 15-6, 19-20
pregnancy and travel, 214-5
Disabilities, travelers with, 220
Disasters, natural, 179-80
Disease, see specific disease names
Disinsection of aircraft, 177
Djibouti
geographic distribution of potential health hazards, 194-5
malaria risk and prophylaxis, by country, 31
yellow fever, by country, 31
Dominica
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 32
yellow fever, by country, 32
Dominican Republic
geographic distribution of potential health hazards, 32
hepatitis B, 91
malaria, 109, 119

malaria risk and prophylaxis, by country, 32
poliomyelitis, 131
yellow fever, by country, 32
Doxycycline
leptospirosis, 105
malaria
adverse reactions, 113, 120
prophylaxis, 110-2, 114-5
plague, 131
Dracunculiasis, 194, 201

E

Easter Island, 203
Ebola hemorrhagic fever, 195
Echinococcosis, 193-4, 198, 200-2
Ecuador
geographic distribution of potential health hazards, 197-8
malaria risk and prophylaxis, by country, 32
onchocerciasis, 129
plague, 130
rabies, 134
yellow fever, 154
yellow fever, by country, 32
Egypt
African sleeping sickness, 59
filariasis, lymphatic, 82
geographic distribution of potential health hazards, 193
hepatitis C, 96
malaria, 109
malaria risk and prophylaxis, by country, 32-3
Rift Valley fever, 139
schistosomiasis, 141
yellow fever, by country, 32-3
El Salvador
geographic distribution of potential health hazards, 196
malaria risk and prophylaxis, by country, 33
rabies, 134
yellow fever, by country, 33
Emerging infectious diseases, 184
Encephalitis/Encephalopathy
African sleeping sickness, 59
bovine spongiform, 61-3
Chagas' disease, 63
diphtheria, tetanus, and pertussis, 73-4
equine, 196
hepatitis A, 90
Japanese, 7, 74-80, 199, 200
malaria, 109
measles, 122
tickborne, 81-2, 201-2
varicella, 150
viral, 197, 203
yellow fever vaccine, 21, 158-9
Entamoeba histolytica, see Amebiasis
Equatorial Guinea
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 33
yellow fever, by country, 33
Eritrea
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 33
yellow fever, by country, 33
Escherichia coli
risks from food and drink, 165
travelers diarrhea, 169-70
Estonia
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 33
yellow fever, by country, 33
Ethiopia
geographical distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 33
meningococcal disease, 125
poliomyelitis, 132
yellow fever, by country, 33
Europe
acquired immunodeficiency syndrome, 58
bovine spongiform encephalopathy, 61-2
cholera, 64
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201-3
hepatitis A, 88
hepatitis B, 93

hepatitis C, 96
hepatitis E, 97
Lyme disease, 105-6
measles, 121
poliomyelitis, 132
rabies, 135
travelers diarrhea, 168
typhus fevers, 149

F

Falkland Islands
geographic distribution of potential health hazards, 198
malaria risk and prophylaxis, by country, 33
yellow fever, by country, 33
Fansidar®
adverse reactions, 112, 120
self-treatment, 117-8
Faroe Islands
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 33
rabies, 135
yellow fever, by country, 33
Fasciolopsiasis, 199
Fiji
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 34
rabies, 135
yellow fever, by country, 34
Filariasis, lymphatic
geographic distribution of potential health hazards, 193-4, 196-200, 203
disease-specific information, 82-3
Finland
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 34
yellow fever, by country 34
Fleas
plague, 130
typhus, 149
Food and Drug Administration (U.S.)
acquired immunodeficiency syndrome, 58
hepatitis B, 95
immunization, reporting adverse events, 12
influenza, 101
rabies, 135
Rift Valley fever, 139
Food safety, 64
France
bovine spongiform encephalopathy, 61
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 34
yellow fever, by country, 34
French Guiana
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 34
yellow fever, by country, 34
French Polynesia
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 34
yellow fever, by country, 34
Futuna Island, 203

G

Gabon
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 34
yellow fever, by country, 34
Gambia, The
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 34
yellow fever, by country, 34
Georgia
geographic distribution of potential health hazards, 200

malaria risk and prophylaxis, by country, 34
yellow fever, by country, 34
Germany
bovine spongiform encephalopathy, 62
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 35
yellow fever, by country, 35
Ghana
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 35
yellow fever, by country, 35
Giardia intestinalis/giardiasis
disease-specific information, 83-4
recreational water, 184
HIV-infected travelers, 208
risk from food and drink, 165, 167
travelers' diarrhea, 170
Gibraltar
malaria risk and prophylaxis, by country, 35
yellow fever, by country, 35
Glucose-6-phosphate dehydrogenase, 115-6
Greece
bovine spongiform encephalopathy, 62
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 35
rabies, 135
yellow fever, by country, 35
Greenland
geographic distribution of potential health hazards, 195
malaria risk and prophylaxis, by country, 35
yellow fever, by country, 35
Grenada
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 35
yellow fever, by country, 35
Guadeloupe
malaria risk and prophylaxis, by country, 35
yellow fever, by country, 35
Guam
encephalitis, Japanese, 79
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 35
rabies, 135
yellow fever, by country, 35
Guatemala
geographic distribution of potential health hazards, 196
hepatitis B, 93
onchocerciasis, 129
malaria risk and prophylaxis, by country, 35
rabies, 134
yellow fever, by country, 35
Guillain-Barré syndrome
hepatitis A, 90
hepatitis B, 95
influenza, 100
Guinea
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 35
yellow fever, by country, 35
Guinea-Bissau
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 35-6
yellow fever, by country, 35-6
Guyana
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 36
yellow fever, by country, 36

H

Haemophilus influenzae type b
disease-specific information, 84
immunization and prophylaxis
adverse reactions, 86

general information, 6-7
infants and younger children, 12-3, 15, 17, 20
travelers with altered immunocompetence, 210
vaccination schedule, 85
Haiti
geographic distribution of potential health hazards, 196-7
hepatitis B, 91
malaria, 109, 119
malaria risk and prophylaxis, by country, 36
yellow fever, by country, 36
Hajj, 125, 201
Halofantrine, 118
Hantavirus, 196, 198
Hemorrhagic fever
Arenavirus, 195, 198
Crimean-Congo, 195, 200-1
death overseas, 187
dengue, 67-9, 197, 203
Ebola, 95
Korean, 199
Lassa, 102
Marburg, 195
tickborne, 200
with renal syndrome, 199, 202
yellow fever, 154
Hepatitis A
acquired immunodeficiency virus, 58
disease specific information, 86-91
vaccines
childhood immunization schedules, 14-5
HAVRIX®, 89
infants and children, 21
immune globulin, 10, 89
pregnancy, 215
VAQTA®, 89
Hepatitis B
acquired immunodeficiency virus, 58
disease-specific information, 91-5
Haemophilus influenzae type B, 84-6
vaccines
adverse reactions, 94-5
immune globulin, 10
infants and children, 13, 15, 18-20
pregnancy, 215
recommendations, 94
Hepatitis C, 96-7
Hepatitis D, 198
Hepatitis E
disease-specific information, 97
geographic distribution of potential health hazards, 193-4, 196, 199, 200
pregnancy, 212
Herpes zoster, see Varicella
Hib, see *Haemophilus influenzae* type B
Hispaniola, 107
Histoplasmosis, 209
HIV, see Human immunodeficiency virus
Honduras
geographic distribution of potential health hazards, 196
hepatitis B, 93
malaria risk and prophylaxis by country, 37
yellow fever, by country, 37
Hong Kong
encephalitis, Japanese, 78
geographic distribution of potential health hazards, 198
rabies, 135
Human immunodeficiency virus
acquired immunodeficiency syndrome (AIDS), 57-9
adoption, international, 222
general travel information
pregnancy, 212
specific precautions, 207-9
vaccine recommendations, 209-11
hepatitis A, 90
influenza, 99, 101
measles, 10, 123
sexually transmitted diseases (STDs), 142
tuberculosis, 145
typhoid fever, 147
World Health Organization blood transfusion guidelines, 186-7
yellow fever, 153
Hungary
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 37
yellow fever, by country, 37
Hydrophobia, see Rabies

Hydroxychloroquine
adverse reactions, 119
prophylaxis, 111, 113

I

Iceland
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 37
yellow fever, by country, 37
Immune globulin
hepatitis A, prevention, 86, 89-91
hepatitis B, prevention, 94
hepatitis E, prevention, 97
HIV-infected travelers, 208
measles, simultaneous administration, 124
pregnancy, 214-5, 217
rabies, 134-5, 138
varicella, simultaneous administration, 153-54
yellow fever, simultaneous administration, 159
Immunocompromised/immunosuppression
hepatitis A, 90
hepatitis B, 94
HIV-infected travelers, 207-9
influenza, 99
measles, 123-24
poliomyelitis, 133
travelers' diarrhea, 172
typhoid, 147
varicella, 153
yellow fever, 158
Immunogenicity
diphtheria, tetanus, and pertussis, 72
measles, 123
typhoid fever, 148-9
vaccination and prophylaxis, 7, 9
varicella, 153
Immunoglobulin, see Immune globulin
Impetigo, 91
India/Indian subcontinent
encephalitis, Japanese, 76
geographic distribution of potential health hazards, 200
hepatitis C, 96
hepatitis E, 97
leishmaniasis, 103
malaria, 107
malaria risk and prophylaxis, by country, 37
plague, 130
poliomyelitis, 132
rabies, 134
typhoid fever, 147
typhus fevers, 149
yellow fever, by country, 37
Indonesia
cholera, 64
encephalitis, Japanese, 77
geographic distribution of potential health hazards, 199-200
hepatitis B, 91
hepatitis E, 97
malaria risk and prophylaxis, by country, 37
plague, 130
yellow fever, by country, 37
Infants
animal-associated hazards, 183
breast-feeding, 212-4
Chernobyl, 181
dengue, 69
diphtheria, tetanus, and pertussis, 70-4
encephalitis, Japanese, 75
Haemophilus influenzae type b, 84-6
hepatitis B, 88, 94
HIV-infected travelers, 207-11
influenza, 98-101
malaria, 112-3, 116-7, 120
measles, 121-3
meningococcal disease, 125, 127
mosquitoes and other arthropod vectors, 164
mumps, 128
plague, 131
poliomyelitis, 132
rabies, 138
rubella, 139-40
travelers' diarrhea, 171, 174-5
tuberculosis, 145
typhoid fever, 147
vaccine recommendations, 12-21
varicella, 150-4
yellow fever, 158
Influenza, 98-102
Injecting drug use
hepatitis B, 91
hepatitis C, 96
immunization schedule, 19
sexually transmitted diseases, 143

Injuries, 181-2
Insect repellent(s)
African sleeping sickness, 59
animal-associated hazards, 182
encephalitis
Japanese, 80
tickborne, 81
leishmaniasis, 103
malaria, 109
protection against mosquitoes and other arthropod vectors, 165
plague, 131
pregnancy
malaria, 218
travel health kit, 220
Rift Valley fever, 139
yellow fever, 160
Insecticides
encephalitis, Japanese, 80
leishmaniasis, 104
malaria, 111
protection against mosquitoes and other arthropod vectors, 164
yellow fever, 160
International certificate of vaccination
vaccination certificate requirements, 3-6
yellow fever, 155, 159
International Health Regulations
smallpox, 144
vaccinations, required/recommended, 3-4
yellow fever, 155, 158-9
IPV, see Poliovirus
Iran
geographic distribution of potential health hazards, 200
malaria risk and prophylaxis, by country, 38
plague, 130
yellow fever, by country, 38
Iraq
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 38
yellow fever, by country, 38
Ireland
bovine spongiform encephalopathy, 61
malaria risk and prophylaxis, by country, 38
rabies, 135
yellow fever, by country, 38
Isle of Man
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 51
rabies, 135
yellow fever, by country, 51
Israel
geographic distribution of potential health hazards,
hepatitis B, 91, 93
malaria risk and prophylaxis, by country, 38
yellow fever, by country, 38
Italy
bovine spongiform encephalopathy, 62
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 38
rabies, 135
yellow fever, by country, 38

J

Jamaica
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 38
rabies, 135
yellow fever, by country, 38
Japan
acquired immunodeficiency syndrome, 58
encephalitis, Japanese, 75-6, 80
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 198-9
hepatitis A, 88
hepatitis B, 93
malaria risk and prophylaxis, by country, 38
rabies, 135
typhus fevers, 149
yellow fever, by country, 38

Japanese encephalitis, see Encephalitis, Japanese
Jordan
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 38
yellow fever, by country, 38

K

Kaolin-pectin
travelers diarrhea, 172
travelers diarrhea during pregnancy, 219
Kazakhstan
geographic distribution of potential health hazards, 200
hepatitis E, 97
malaria risk and prophylaxis, by country, 38
plague, 130
yellow fever, by country, 38
Kenya
geographic distribution of potential health hazards, 194
malaria, 117
malaria risk and prophylaxis, by country, 38
plague, 130
Rift Valley fever, 139
yellow fever, by country, 38
Kiribati
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 39
rabies, 135
yellow fever, by country, 39
Korea
encephalitis, Japanese, 75, 77
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 199
hepatitis B, 91
North
geographic distribution of potential health hazards, 198
malaria risk and prophylaxis, by country, 39
yellow fever, by country, 39
South
geographic distribution of potential health hazards, 198-9
malaria risk and prophylaxis, by country, 39
yellow fever, by country, 39
typhus fevers, 149
Korean hemorrhagic fever, see Hemorrhagic fever, Korean
Kuwait
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 39
rabies, 135
yellow fever, by country, 39
Kyrgyzstan
geographic distribution of potential health hazards, 200
malaria risk and prophylaxis, by country, 39
yellow fever, by country 39

L

Laos
encephalitis, Japanese, 77
malaria risk and prophylaxis, by country, 39
plague, 130
yellow fever, by country, 39
Lassa fever
disease-specific information, 102
geographic distribution of potential health hazards, 195
Latvia
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 39
yellow fever, by country, 39
Lebanon
geographic distribution of potential health hazards, 201

malaria risk and prophylaxis, by country, 39
yellow fever, by country, 39
Leishmaniasis
cutaneous
disease-specific information, 103
geographic distribution of potential health hazards, 194, 196-8, 200-2
disease-specific information, 103
geographic distribution of potential health hazards, 193
mucocutaneous, 196-7
visceral
disease-specific information, 103
geographic distribution of potential health hazards, 194, 196-8, 200-2
specific precautions for HIV-infected travelers, 209
Leptospirosis
disease-specific information, 104-5
geographic distribution of potential health hazards, 199
Lesotho
geographic distribution of potential health hazards, 199
malaria risk and prophylaxis, by country, 39
yellow fever, by country, 39
Liberia
geographic distribution of potential health hazards, 194
Lassa fever, 102
malaria risk and prophylaxis, by country, 39
poliomyelitis, 132
yellow fever, by country, 39
Libya
African sleeping sickness, 59
geographic distribution of potential health hazards, 193
malaria risk and prophylaxis, by country, 39
plague, 130
rabies, 135
yellow fever, by country, 39
Liechtenstein
bovine spongiform encephalopathy, 61
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 39
yellow fever, by country, 39
Listeria, 219
Lithuania
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 39
yellow fever, by country, 39
Live virus vaccine, see Vaccine
Luxembourg
bovine spongiform encephalopathy, 61
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 40
yellow fever, by country, 40
Lyme disease
disease-specific information, 105-6
geographic distribution of potential health hazards, 196, 201-2
Lymphatic filariasis, see Filariasis
Lymphedema, see Filiariasis

M

Macao, 198-9
Macedonia, the Former Republic of
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 40
yellow fever, by country, 40
Madagascar
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 40
plague, 130
yellow fever, by country, 40
Madeira
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 40
yellow fever, by country, 40
Malaria
disease-specific information, 106-20
chemoprophylaxis
adverse reactions, 119-20
general, 111-7, 137

infants, children, and adolescents, 112
pregnancy, 113
HIV-infected travelers, 208
leptospirosis, 104
mosquitoes and other arthropod vectors, 163-65
pregnancy, 123
rabies, 137
risk and prophylaxis, by country, 23-54
self-treatment, 117-9
typhoid fever, 148-9
varicella, 154
yellow fever, 159
Malarone™, see atovaquone/proguanil
Malawi
geographic distribution of potential health hazards, 194
malaria, 117
malaria risk and prophylaxis, by country, 40
plague, 130
yellow fever, by country 40
Malaysia
encephalitis, Japanese, 76-7
geographic distribution of potential health hazards, 199-200
hepatitis E, 97
malaria risk and prophylaxis, by country, 40
rabies, 135
yellow fever, by country 40
Maldives
geographic distribution of potential health hazards, 200
malaria risk and prophylaxis, by country, 40
rabies, 135
yellow fever, by country 40
Mali
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 40
meningococcal disease, 125
yellow fever, by country, 40
Malta
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 41
rabies, 135
yellow fever, by country, 41
Marburg hemorrhagic fever, see Hemorrhagic, fever
Marshall Islands
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 41
yellow fever, by country, 41
Martinique
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 41
rabies, 135
yellow fever, by country, 41
Mauritania
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 41
Rift Valley fever, 139
yellow fever, by country, 41
Mauritius
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 41
rabies, 135
yellow fever, by country 41
Mayotte, 41
Measles
disease-specific information, 121-4
HIV-infected travelers, 208-11
pregnancy and breast-feeding, 213-5
vaccine
adverse reactions, 122-4
MMR, 121-3
rubella, 140-1
varicella, 152, 154
yellow fever, 159
Mefloquine
adverse reactions, 119-20
breast-feeding, 116
infants, children, and adolescents, 112-3
malaria, 109-20
pregnancy, 113, 218-9
prophylaxis, 111-4

rabies, 137
self-treatment, 118
simultaneous administration, 7
typhus, 148-9
Melanesia
geographic distribution of potential health hazards, 203
leishmaniasis, 103
Melioidosis, 199
Meningitis/meningococcal disease
disease-specific information, 124-7
geographic distribution of potential health hazards, 195, 198-200
Hajj, 125
pregnancy and travel, 215, 217
Mexico
geographic distribution of potential health hazards, 196
Chagas' disease, 63
dengue hemorrhagic fever, 67
hepatitis A, 87
hepatitis B, 93
hepatitis E, 97
malaria, 107
malaria risk and prophylaxis, by country, 41
onchocerciasis, 129
rabies, 134
yellow fever, by country, 41
Microfilaria
filariasis, 82-3
onchocerciasis, 129
Micronesia (Federates States of)
geographic distribution of potential health hazards, 203
leishmaniasis, 103
malaria risk and prophylaxis, by country, 42
yellow fever, by country, 42
Middle East
animal-associated hazards, 183
geographic distribution of potential health hazards, 200-1
hepatitis B, 91
hepatitis C, 96
hepatitis E, 97
leishmaniasis, 103
malaria, 107, 109
travelers' diarrhea, 168
Military orders (travel on), 5
Mite-borne infections, 163
MMR, see Measles
Moldova
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 42
yellow fever, by country, 42
Monaco
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 42
rabies, 135
yellow fever, by country, 42
Mongolia
geographic distribution of potential health hazards, 198-9
malaria risk and prophylaxis, by country, 42
yellow fever, by country, 42
Monkeypox, see Smallpox
Montserrat
geographic distribution of potential health hazards, 197
rabies, 135
yellow fever, by country, 42
Morocco
geographic distribution of potential health hazards, 193
malaria risk and prophylaxis, by country, 42
yellow fever, by country, 42
Mosquitoes
dengue, 67
disinsection, 177
HIV-infected travelers, 209
encephalitis, Japanese, 74
filariasis, lymphatic, 82
malaria, 109, 111
protection against, 163-5
Rift Valley fever, 139
yellow fever, 158-60
Motion sickness, 163
Motor vehicle accidents/crashes
injuries, 181
pregnant travelers, 212
Mozambique
geographic distribution of potential health hazards, 194
malaria, 117

malaria risk and prophylaxis, by country, 42
plague, 130
yellow fever, by country, 42
Mumps
disease-specific information, 127-8
general recommendations on vaccination and prophylaxis, 6-7
HIV-infected travelers, 209
inadequately immunized infants and younger children, 12-3, 15-7, 19-20
measles, 121-4
rubella, 140, 152, 154
vaccine, 128, 214-5
Murine typhus, see Typhus
Myanmar, see Burma
Mycobacterium tuberculosis, see Tuberculosis

N

N,N-diethylmetatoluamide
dengue, 69
encephalitis, tickborne, 82
infants and children, 164
leishmaniasis, 103
malaria, 109
plague, 131
pregnancy, 218
protection against mosquitoes and other arthropod vectors, 164
yellow fever, 160
Namibia
geographic distribution of potential health hazards, 195
malaria risk and prophylaxis, by country, 42
yellow fever, by country, 42
Nauru
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 43
yellow fever, by country, 42
Neisseria gonorrhoeae, see Sexually transmitted diseases
Neomycin, 9, 122, 133, 153
Nepal
cyclosporiasis, 66
encephalitis, Japanese, 77
geographic distribution of potential health hazards, 200
leishmaniasis, 103
malaria risk and prophylaxis, by country, 43
poliomyelitis, 132
rabies, 134
yellow fever, by country, 43
Netherlands
bovine spongiform encephalopathy, 61
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 43
yellow fever, by country 43
Netherlands Antilles
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 43
rabies, 135
yellow fever, by country, 43
New Caledonia
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 43
rabies, 135
yellow fever, by country, 43
New Zealand
acquired immunodeficiency syndrome, 58
geographic distribution of potential health hazards, 203
hepatitis A, 88
hepatitis B, 93
malaria risk and prophylaxis, by country, 43
rabies, 135
travelers' diarrhea, 168
yellow fever, by country, 43
Nicaragua
geographic distribution of potential health hazards, 196
malaria risk and prophylaxis, by country, 43
yellow fever, by country, 43
Niger
geographic distribution of potential health hazards, 194

malaria risk and prophylaxis, by country, 43
yellow fever, by country, 43
Nigeria
geographic distribution of potential health hazards, 194
Lassa fever, 102
malaria risk and prophylaxis, by country, 43
poliomyelitis, 132
yellow fever, by country 43
Niue
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 43
yellow fever, by country, 43
North Africa
cholera, 64
geographic distribution of potential health hazards, 193
North America/Americas
dengue, 76, 69
geographic distribution of potential health hazards, 195
hepatitis B, 93
hepatitis C, 96
influenza, 98
leishmaniasis, 103
Lyme disease, 106
plague, 130
typhus, 149
Northern Mariana Islands, 43
Norwalk(-like) virus
recreational water, 184
risks from food and drink, 165
travelers' diarrhea, 170
Norway
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 44
rabies, 135
yellow fever, by country 44

O

Obstetrical risk factors, see Pregnancy
Oceania
geographic distribution of potential health hazards, 203
leishmaniasis, 103
malaria, 107
rabies, 135
Oman
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 44
yellow fever, by country, 44
Onchocerciasis, 129
OPV, see Poliovirus, oral
Oral rehydration salts (ORS), 173-4
Oriental liver fluke, 199
Oriental lung fluke, 194, 198-9
Orthopox viruses, see Smallpox

P

Pacific islands
filariasis, lymphatic, 82
hepatitis B, 91
leishmaniasis, 103
Pacific Islands, U.S. Trust Territory
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 44
yellow fever, by country, 44
Pakistan
encephalitis, Japanese, 77
geographic distribution of potential health hazards, 200
hepatitis E, 97
malaria risk and prophylaxis, by country, 44
poliomyelitis, 132
yellow fever, by country 44
Palau
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 44
rabies, 135
yellow fever, by country, 44
Panama
geographic distribution of potential health hazards, 196

malaria, 109
malaria risk and prophylaxis, by country, 44
yellow fever, by country, 44
Papua
encephalitis, Japanese, 77
yellow fever, by country, 37
Papua New Guinea
encephalitis, Japanese, 77
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 44
rabies, 135
yellow fever, by country, 44
Paragonimiasis, 194, 198-9
Paraguay
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 45
yellow fever, by country, 45
Parasitic Diseases Drug Service, 83
Passive immunization, 12
Penicillium marneffei, 209
Permethrin
encephalitis, tickborne, 82
leishmaniasis, 104
malaria, 109, 111
malaria during pregnancy, 218
mosquitoes and other arthropod vectors, 164-5
plague, 131
Rift Valley fever, 139
yellow fever, 160
Pertussis
disease-specific information, 70-4
emerging infectious diseases, 184
geographic distribution of potential health hazards, 196
Haemophilus influenzae type B, 84-6
hepatitis B, 95
inadequately immunized infants and children, 12-3, 15-6, 19-20
vaccine/vaccination
general recommendations, 3, 6
HIV-infected travelers, 210
simultaneous administration, 7
Peru
cholera, 64
geographic distribution of potential health hazards, 197-8
plague, 130
malaria risk and prophylaxis, by country, 45
rabies, 134
yellow fever, 154
yellow fever, by country, 45
Pets, see Animal Importation or Reentry
Philippines
geographic distribution of potential health hazards, 199-200
encephalitis, Japanese, 78
hepatitis B, 91
malaria risk and prophylaxis, by country, 45
rabies, 134
schistosomiasis, 141
yellow fever, by country, 45
Pitcairn Islands
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 45
yellow fever, by country 45
Plague
death overseas, 186
disease-specific information, 130-1
geographic distribution of potential health hazards, 194-9, 199-200
vaccine, 130-1
Plasmodium
falciparum
geographic distribution of potential health hazards, 194
malaria, 106, 110, 114
malaria during pregnancy, 213
malariae, 106
ovale, 106
vivax, 106
Pneumocystis carinii pneumonia, 208
Poland
bovine spongiform encephalopathy, 81
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 45
yellow fever, by country 45

Poliomyelitis/poliovirus
disease-specific information, 131-3
vaccine
inactivated
adverse reactions, 133, 209
general recommendations on vaccination and prophylaxis, 12, 13, 15, 17, 19, 20
HIV-infected travelers, 209-10
pregnancy and travel, 214-6
simultaneous administration, 7
oral
adverse reactions, 12
HIV-infected travelers, 211
pregnancy and travel, 214
Portugal
bovine spongiform encephalopathy, 61-2
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 45
rabies, 135
yellow fever, by country, 45
Pregnancy/pregnant women
altitude illness, 179
air travel, 219-20
breast-feeding and travel, 211-4
dengue hemorrhagic fever, 69
diphtheria-tetanus, 214
encephalitis, Japanese, 80, 217
factors affecting the decision to travel, 211
general recommendations and relative contraindications, 211-4
guidelines for pregnant travelers, 212
hepatitis A, 91, 216-7
hepatitis B, 95, 216
hepatitis E, 97
influenza, 99, 101, 216
malaria, 110, 113-16, 120, 218
measles (MMR), 123, 214
meningococcal disease, 127, 217
motor vehicle accidents, 212
obstetrical risk factors, 213
poliomyelitis, 133, 214, 216
rabies, 138, 217
rubella, 139-40
HIV-infected travelers, 208
travel health kit, 220
travelers' diarrhea, 174, 218-9
typhoid fever, 147, 217
vaccination during, 215-6
varicella, 153
yellow fever, 158, 216
Primaquine
malaria treatment, 115-6, 119-20
pregnancy, 219
Puerto Rico
Dengue Branch, CDC, 69
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 45
yellow fever, by country, 45
Purified protein derivative (PPD)
measles, 124
varicella, 154

Q

Qatar
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 46
rabies, 135
yellow fever, by country, 46
Quarantine, Division of, 189

R

Rabies
animal-associated hazards,182
disease-specific information, 133-8
geographic distribution of potential health hazards, 193, 195-203
HIV-infected travelers, 209
importation or reentry of pets, 187-8
pregnancy, 215, 217
vaccination and prophylaxis, 3, 10, 119, 134-8
Repellent(s), see Insect repellent(s)
Réunion
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 46
rabies, 135
yellow fever, by country, 46
Reye's syndrome
influenza, 99

travelers' diarrhea, 171
varicella, 154
Rickettsiae, 149
Rift Valley fever
disease-specific information, 139
geographic distribution of potential health hazards, 193, 195
Risks from food and drink, 165-8
River blindness, see Onchocerciasis
Rocky Mountain spotted fever, 196
Rodent
fleas, 130
mites, 149
Rodent-borne diseases
arenavirus hemorrhagic fevers, 198
hantavirus,196
Korean hemorrhagic fever, 199, 202
Romania
bovine spongiform encephalopathy, 81
geographic distribution of potential health hazards, 202-3
malaria risk and prophylaxis, by country, 46
yellow fever, by country, 46
Rubella
disease-specific information, 139-41
general recommendation on vaccination and prophylaxis, 6-7, 12
geographic distribution of potential health hazards, 196
HIV-infected travelers, 209
infants and children, 12-3, 15-7, 19-20
measles/MMR, 121-4
pregnancy, 214-5
varicella, 154
Russia
Chernobyl, 180
diphtheria, 70
encephalitis, Japanese, 75, 78
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201-2
hepatitis B, 93
malaria risk and prophylaxis, by country, 46
plague, 130
typhus fevers, 149
yellow fever, by country, 46
Rwanda
geographic distribution of potential health hazards, 194-5
malaria risk and prophylaxis, by country, 46
yellow fever, by country, 46

S

Saint Christopher and Nevis, see Saint Kitts and Nevis
Saint Eustatius, 135
Saint Helena
malaria risk and prophylaxis, by country, 46
yellow fever, by country, 46
Saint Kitts and Nevis
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 46
rabies, 135
yellow fever, by country, 46
Saint Lucia
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 46
rabies, 135
yellow fever, by country, 46
Saint Martin, 135
Saint Pierre and Miquelon
malaria risk and prophylaxis, by country, 46
yellow fever, by country, 46
Saint Vincent and the Grenadines
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 46
rabies, 135
yellow fever, by country, 46
Salmonella, 169, 172
Salmonella typhi, see Typhoid fever
Salmonellosis
geographic distribution of potential health hazards, 196, 198, 202
importation or reentry of pets, 188
Samoa
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 46

rabies, 135
yellow fever, by country, 46
Samoa, American
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 48
yellow fever, by country, 48
San Marino
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 47
yellow fever, by country, 47
Sand flies, 103-4
São Tomé and Principe
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 47
yellow fever, by country, 47
Saudi Arabia
geographic distribution of potential health hazards, 201
meningococcal disease, 125
plague, 130
malaria risk and prophylaxis, by country, 47
Rift Valley fever, 139
yellow fever, by country, 47
Scandinavia
encephalitis, tickborne, 81
hepatitis C, 96
Schistosomiasis
cercariae, 141
disease-specific information, 141-2
geographic distribution of potential health hazards, 193, 195, 197-201
Scombroid, 168
Scrub typhus
geographic distribution of potential health hazards, 199
typhus, 149-50
Senegal
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 47
yellow fever, by country, 47
Sexually transmitted diseases, 142-3
Seychelles
geographic distribution of potential health hazards, 194-5
malaria risk and prophylaxis, by country, 47
rabies, 135
yellow fever, by country, 47
Shigella/*Shigella dysenteriae*/Shigellosis, 165, 169, 196
Shingles, see Herpes zoster
Sickle-cell disease, 219
Sierra Leone
geographic distribution of potential health hazards, 194
Lassa fever, 102
malaria risk and prophylaxis, by country, 47
poliomyelitis, 132
yellow fever, by country, 47
Simulium flies, 129
Singapore
encephalitis, Japanese, 78
geographic distribution of potential health hazards, 199
malaria risk and prophylaxis, by country, 47
rabies, 135
yellow fever, by country, 47
Sint Maarten, 135
Slovakia
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 48
yellow fever, by country, 48
Slovenia
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 48
yellow fever, by country, 48
Smallpox
death overseas, 186
disease-specific information, 144
Snakes
geographic distribution of potential health hazards, 193, 196, 198, 200, 203-4
animal-associated hazards, 183

Solomon Islands
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 48
yellow fever, by country, 48
Somalia
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 48
poliomyelitis, 132
smallpox, 144
yellow fever, by country, 48
South Africa
African sleeping sickness, 59
geographic distribution of potential health hazards, 195
hepatitis C, 96
malaria, 117
malaria risk and prophylaxis, by country, 48
plague, 130
yellow fever, by country, 48
South America/Americas
animal-associated hazards, 183
dengue, 67, 69
geographic distribution of potential health hazards, 196-8
hepatitis B, 93
hepatitis E, 97
leishmaniasis, 103
malaria, 107, 109, 117
plague, 130
rabies, 134-5
recreational water, 184
schistosomiasis, 142
typhoid fever, 147
typhus fevers, 149-50
yellow fever, 154-5, 159
Southeast Asia
dengue hemorrhagic fever, 67
hepatitis B, 91
malaria, 107, 117-8
plague, 130
schistosomiasis, 141
Spain
bovine spongiform encephalopathy, 62
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 48
rabies, 135
yellow fever, by country, 48
Spotted fever, 150
Sri Lanka
encephalitis, Japanese, 78
geographic distribution of potential health hazards, 200
malaria risk and prophylaxis, by country, 48
rabies, 134
yellow fever, by country, 48
St., see Saint
Steroid therapy
HIV-infected travelers, 209
varicella, 153
yellow fever, 158
Streptomycin, 133
Sub-Saharan Africa
filariasis, lymphatic, 82
hepatitis E, 97
malaria, 107
meningococcal disease, 125
poliomyelitis, 132
schistosomiasis, 141
Sudan
geographic distribution of potential health hazards, 194
leishmaniasis, 103
malaria risk and prophylaxis, by country, 48
poliomyelitis, 132
yellow fever, by country, 48
Sulfonamide
altitude illness, 179
malaria, 116
Summary of Health Information for International Travel, 3, 21
Suriname
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 49
yellow fever, by country, 49
Swaziland
geographic distribution of potential health hazards, 195
malaria risk and prophylaxis, by country, 49
yellow fever, by country, 49

Sweden
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 49
rabies, 135
yellow fever, by country 49
Switzerland
bovine spongiform encephalopathy, 61
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 49
rabies, 135
yellow fever, by country, 49
Syria
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 49
yellow fever, by country, 49

T

Taeniasis, 198, 201-2
Taiwan
encephalitis, Japanese, 78
geographic distribution of potential health hazards, 198
rabies, 135
Tajikistan
geographic distribution of potential health hazards, 200
hepatitis E, 97
malaria risk and prophylaxis, by country, 49
poliomyelitis,132
yellow fever, by country, 49
Tanzania
geographic distribution of potential health hazards, 194
malaria, 117
malaria risk and prophylaxis, by country, 49
plague, 130
Rift Valley fever, 139
yellow fever, by country, 49
Tattooing
acquired immunodeficiency syndrome, 58
hepatitis B, 91
hepatitis C, 96-7
Tetanus, see also Diphtheria
diphtheria, pertussis, and tetanus, 70-4
general recommendations on vaccination, 3, 6-7, 10, 12
HIV-infected travelers, 209
inadequately immunized infants and younger children, 12-3, 15-6, 19-20
pregnancy, 214-5
Tetracycline
malaria, 113, 116
plague, 131
sexually transmitted diseases, 143
travelers' diarrhea, infants and children, 174
typhus fevers, 149
Thailand
encephalitis, Japanese, 79
geographic distribution of potential health hazards, 199-200
malaria, 109
malaria risk and prophylaxis, by country, 49
rabies, 134
yellow fever, by country, 49
Tick(s)
encephalitis, tickborne, 81-2
geographic distribution of potential health hazards, 194, 202
Lyme disease, 105-6
mosquitoes and other arthropod vectors, 163-4
typhus, 150
Tick-bite fever, 195
Tickborne relapsing fever, 200-1
Togo
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 49
yellow fever, by country, 49
Tokelau
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50

Tonga
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50
Toxoid(s)
diphtheria, 72
general recommendations on vaccination and prophylaxis, 6-7, 9, 12
pregnancy, 214
vaccine recommendations for infants and children, 12-3, 15-6, 19-20
Toxoplasmosis, 219
Trachoma, 193, 195, 199-201, 204
Transplacental infection, 63, 116
Transverse myelitis
hepatitis A, 90
schistosomiasis, 141
Travel health kit, 220
Travelers' diarrhea
disease-specific information, 168-75
HIV-infected travelers, 208
pregnancy, 218-20
Trichinellosis, 202
Trimethoprim-sulfamethoxazole, see also Sulfonamide
HIV-infected travelers, 208
plague, 131
travelers' diarrhea, 171
Trinidad and Tobago
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50
Trypanosomiasis
African, see African sleeping sickness
American, see Chagas' disease
Tsetse flies, 59-60
Tuberculosis
adoption, international, 222
death overseas, 186-7
disease-specific information, 144-6
emerging infectious diseases, 184
measles,
HIV-infected travelers, 209
pregnancy, 217
tuberculin testing (see also Purified protein derivative [PPD]), 124, 154
Tularemia, 196-7
Tungiasis, 194
Tunisia
geographic distribution of potential health hazards, 193
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50
Turkey
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50
Turkmenistan
geographic distribution of potential health hazards, 200
hepatitis E, 97
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50
Turks and Caicos Islands, 197
Turtles, see Animal Importation or Reentry
Tuvalu
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50
Typhoid fever
disease-specific information, 146-9
geographic distribution of potential health hazards, 193-6, 198-203
HIV-infected travelers, 209
measles, 122
natural disasters and environmental hazards, 180
risk from food and drink, 165
vaccine/vaccination
adverse reactions, 147-8
general recommendations on vaccination and prophylaxis, 3, 7
infants and children, 18
people with acute illness, 8
pregnancy, 215, 217
Typhus fevers
disease-specific information, 149-50
endemic/murine, 202
geographic distribution of potential health hazards, 193, 195, 197, 199-200
leptospirosis, 104

scrub, 199
tick/tickborne, 194-5, 201-2

U

Uganda
geographic distribution of potential health hazards, 194
malaria, 117
malaria risk and prophylaxis, by country, 50
plague, 130
yellow fever, by country, 50
Ukraine
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 201-2
malaria risk and prophylaxis, by country, 50
yellow fever, by country, 50
United Arab Emirates
geographic distribution of potential health hazards, 201
malaria risk and prophylaxis, by country, 51
rabies, 135
yellow fever, by country, 51
United Kingdom
bovine spongiform encephalopathy, 61-2
geographic distribution of potential health hazards, 201
hepatitis C, 96
malaria risk and prophylaxis, by country, 51
rabies, 135
smallpox, 144
yellow fever, by country, 51
United States
acquired immunodeficiency syndrome, 58-9
animal importation or reentry, 188-9
cholera, 64
death overseas, 187
dengue, 67, 69
diphtheria, tetanus, and pertussis, 71
encephalitis, Japanese, 75
filariasis, lymphatic, 82
geographic distribution of potential health hazards, 195-6
hepatitis A, 88, 90-1
hepatitis B, 93, 95
hepatitis C, 96
illness abroad, 185
immunizations recommendations and schedules for infants and children, 13-5, 19-20
influenza, 98-100
leishmaniasis, 103
Lyme disease, 105-6
malaria, 107, 111, 113
malaria risk and prophylaxis, by country, 51
measles, 121
meningococcal disease, 125
mumps, 127-8
plague, 130
poliomyelitis, 131-2
rabies, 134
risks from food and drink, 165, 168
rubella, 140
travelers' diarrhea, 168, 174
tuberculosis, 144-6
vaccination certificate requirements, 4-6
varicella, 151
yellow fever, by country, 51
Uruguay
geographic distribution of potential health hazards, 198
malaria risk and prophylaxis, by country, 51
rabies, 135
yellow fever, by country, 51
Uzbekistan
geographic distribution of potential health hazards, 198
hepatitis E, 97
malaria risk and prophylaxis, by country, 51
yellow fever, by country, 51

V

Vaccine(s)/Vaccination
cruise ship travel, 175
exemption, 5
general information regarding HIV and travel, 207-11

general recommendations, 6-21
HIV-infected travelers, 209-11
infants and children, 12-21
pregnancy, 211-7
travelers' diarrhea, 171
Vaccine Adverse Event Reporting System
general recommendations on vaccination and prophylaxis, 12
hepatitis B vaccine, 95
yellow fever vaccine, 158
Vaccinia, 144
Vanuatu
malaria risk and prophylaxis, by country, 51
rabies, 135
yellow fever, by country, 51
Varicella
disease-specific information, 150-4
measles, 124
vaccine/vaccination
adverse reactions, 152-4
disease-specific information, 151-4
general recommendations, 6-8, 12
HIV-infected travelers, 210
inadequately immunized infants and younger children, 12-3, 15, 17, 19-20
pregnancy, 153-4
Venezuela
dengue hemorrhagic fever, 67
geographic distribution of potential health hazards, 199-200
malaria risk and prophylaxis, by country, 51
onchocerciasis, 129
yellow fever, by country, 51
Venezuelan equine encephalitis, 196
Vibrio cholerae, 170
Vietnam
encephalitis, Japanese, 79
geographic distribution of potential health hazards, 199-200
malaria risk and prophylaxis, by country, 51
plague, 130
rabies, 134
yellow fever, by country, 51
Virgin Islands
geographic distribution of potential health hazards, 197
malaria risk and prophylaxis, by country, 51
rabies, 135
yellow fever, by country, 51

W

Wake Island
geographic distribution of potential health hazards, 203
malaria risk and prophylaxis, by country, 51
yellow fever, by country, 51
Water, filters and treatment, 65-6, 165-7
World Health Organization
blood transfusion guidelines for international travelers, 185-6
bovine spongiform encephalopathy, 61
cholera, 64
disinsection, 177
international travel for inadequately immunized infants and younger children, 21
malaria, 107, 110
Oral rehydration salts, 173-4
smallpox, 144
tuberculosis, 145
yellow fever, 155

Y

Yellow fever
death overseas, 186
disease-specific information, 155-60
geographic distribution of potential health hazards, 194, 197
HIV-infected travelers, 209, 211
measles, 122
mosquitoes and other arthropod vectors, 163
pregnancy, 213, 215-6
typhoid, 149
vaccine requirements, by country, 23-54
varicella, 152
Yemen
geographic distribution of potential health hazards, 201

malaria risk and prophylaxis, by country, 51
onchocerciasis, 129
plague, 130
Rift Valley fever, 139
yellow fever, by country, 51
Yugoslavia
encephalitis, tickborne, 81
geographic distribution of potential health hazards, 202
malaria risk and prophylaxis, by country, 51
yellow fever, by country, 51

Z

Zambia
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 52
plague, 130
yellow fever, by country, 52
Zimbabwe
geographic distribution of potential health hazards, 194
malaria risk and prophylaxis, by country, 52
plague, 130
yellow fever, by country 52